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THE TEACHING OF PATHOLOGICAL PHYSIOLOGY.
III.[1]
ORGANS OF RESPIRATION.

By W. G. MacCallum, M. D.

(From the Hunterian Laboratory, Johns Hopkins University, Baltimore.)

In the third session of this course, the aims and objects of which need not be again stated, the diseased conditions of the organs of respiration were selected for study, and attention was directed not especially to those conditions caused by infectious agencies which can be studied to far greater advantage at the autopsy table and in the wards, but rather to those numerous disturbances which are of a mechanical nature and which thus lend themselves to experimental study. Indeed with few exceptions these pathological or disturbed conditions form a large part of what we find described in the text books on physiology, so dependent is the physiologist on interfering with the smooth working of organs in order to learn from their behavior in adversity what they have really been doing in time of peace. So it is, too, with the anatomist who is so often found depending upon the study of abnormalities to teach him the normal and who finds that the school book pictures of histological structure, often so difficult to see, come out with startling clearness in a pathologically altered tissue.

Especially interesting in the mechanism of respiration in mammals is the arrangement of the structures which by their

[1] On the Teaching of Pathological Physiology, I and II, J. H. H. Bulletin, Aug. 1906, and Sept., 1907.

movements draw in and expel the air from the lung. It is needless to describe this mechanism here except perhaps in so far as to point out the variations in the enlargement of the chest in different regions which inevitably result from the shape of the ribs, and from the character and direction of the hinge about which they rotate. This is such that the increase in volume of the upper portion of the chest is largely in the antero-posterior direction since the axis of rotation of the upper ribs approaches a line parallel with the anterior surface of the body, for this axis is the line between the two articulations of the ribs to the centrum and the transverse process of the vertebra. In the lower ribs the articulation is between similar points but the transverse process is bent so far backward that the axis of rotation of the rib is more nearly perpendicular to the anterior surface of the body. Thus it happens that in the lower part of the chest the enlargement is chiefly lateral. There, too, the enlargement is far greater, because since any approach on the part of a rib to a position at right angles to the vertebra must enlarge the space it surrounds, the upper ribs hanging as they do much nearer that position than the greatly slanted lower ribs do not so greatly enlarge the enclosed space by a movement of a certain distance as do the more oblique ones. All this movement is associated with some forward movement of the sternum, but that seems not so great as the up and down movement of that bone. At least in dogs when the movement of various points on the sternum was recorded it was found that aside from the up and down movement the forward protrusion is slight anywhere but is much greater at the lower than at the upper end; at the angle of Ludwig it is perhaps least. The curves recorded from tambours attached at intervals of 4 cm. along the sternum show this well. Similar curves taken from the ribs laterally showed the greatest variation in the extent of the movements which change the volume of the thorax. It is difficult to describe briefly these differences and it would be even more difficult to represent them graphically as it was planned to do by means of a series of recording levers showing the curves simultaneously produced from all parts of the thorax. As pointed out by Tendeloo, it is apparent that the volume of the thorax changes least near the spine; laterally and especially low down in the thorax it varies most while antero-posteriorly the variation is relatively great in the upper part of the chest.

In watching the respiratory changes the impression is gained that the whole expansion of the chest is not synchronous but proceeds, as Hutchinson suggested, in a wave-like form from above downward. The muscular mechanism bringing about these movements may be studied by electrical stimulation of the exposed muscles although there is a difference between the results of such isolated stimuli and the concerted action of all the muscles.

To all this is added the synchronous action of the diaphragm which produces so great a variation in the volume of the thorax from below, pulling in the ribs in inspiration along its line of attachment, although at the same time by compressing the abdominal contents the lowermost ribs are forced out.

Through the opened abdomen one can follow the movements of the diaphragm, with its passive central tendon which is transparent enough to show the pale pink lung sliding up and down, following into the space opened by the contraction of the diaphragm away from the chest wall. The excursion is not a very great one, however, and if the pleura between the ribs be exposed the lung can be seen through it. There too it moves up and down a little, sliding on the pleura and adhering closely. It does not move far and apparently the movement is less marked as we pass upward, although this should be accurately measured.

The question then arises as to the effect which this great inequality in the change in volume, in different parts of the thorax, may have upon the changes in pressure in different regions. As is well known many efforts have been made to compare the intrapleural pressure in different parts of the thorax by the most various procedures and Tendeloo in his monograph discusses these and in effect bases most of his explanations of mechanical changes in the lungs upon the theory that certain portions of the lung are subject to greater variations of pressure than others. This subject will be discussed in detail by members of the class who devoted themselves especially to its study. That alterations in pressure in one part of the thoracic cavity need not be felt in other distant parts seems to be true to a certain degree and to depend upon the adhesion between the pleural surfaces which will slide easily upon one another but which do not transmit changes in pressure unaltered. This can be exemplified by a rubber balloon with wet surface inside a bottle which has a side neck. If the neck of the balloon be on a glass tube which passes through a tight cork in the bottle and air be sucked out at the side neck the whole balloon will expand. If, however, the wet surface of the balloon touches the walls of the bottle in such a way as to cover the orifice of the side neck and suction now be made there, the whole balloon will not expand but only that part which covers the mouth of the side neck, for the wall of the balloon sticks to the wall of the bottle and pressure is not lowered in the rest of the cavity of the bottle around the balloon. The experiments which were made to prove the different variations in pressure in distant parts of the thorax will be recounted in the paper mentioned. That this must necessarily result in differences in the degree of expansion of different portions of the lung is obvious and doubtless has its important bearing upon the well-known common apical localization of tuberculosis.

It is possible to study a number of mechanical disturbances of respiration such as occur frequently in human beings and these are interesting when the blood pressure in various parts of the circulatory system as well as the respiratory movements and thoracic pressure relations can be recorded. For instance, a pleural effusion produced by injecting water or oil into the pleura, disturbs the respiratory movements greatly, as is seen in the curves. Intrapleural pressure becomes positive and the

lungs are blanched and compressed while the arterial pressure sinks and the venous pressure is increased.

The general relations of the circulatory conditions to respiration can be made more striking by thus increasing the intrapleural pressure, say by introducing a quantity of air into the pleural cavity. Violent respiratory efforts follow which are of little avail since they do not expand the lungs. They are, however, associated with great waves in the blood pressure curves which are synchronous with the respiratory movements but may be due in part at any rate to coincident vasomotor stimuli. The expulsion of the air reduces the condition to the normal again and the old relations are restored. This experiment may be regarded as representing the conditions in closed pneumo-thorax but the types of valvular pneumo-thorax may easily be imitated by inserting a tube into the thoracic wall with a valve working only one way. Air soon accumulates in the pleura to such an extent that respiration is impossible. In this respect the condition in the dog differs from that in man, since except for the most delicate membrane the two pleural cavities are practically one and changes in pressure in one are immediately felt in the other. For the same reason it is difficult to represent open pneumo-thorax in the dog.

Inflation of the abdomen produced only a costal type of respiration with rather shallow respirations and no especial change in the circulatory relations.

Other mechanical obstructions to respiration were, however, readily reproduced and the symptoms studied. Stenosis of the trachea and valvular obstruction to the trachea or larynx such as might result from the presence of a pedunculated tumor, a loose diphtheritic membrane, or certain forms of paralysis of the vocal cords, give very characteristic changes in the respiratory movements which are so familiar that it is not necessary to discuss them here. The relations of the intrapleural pressure to these obstructions of the trachea are, however, interesting and will be separately described. It was found, as might be expected, that under some circumstances the obstruction in the trachea may raise the intrapleural pressure above that of the atmosphere. This has been much discussed by Aron and Reichmann in their efforts to determine the mode of action of cough upon the peripheral parts of the lung and bronchioles, and we lean toward the view of Reichmann that a positive intrapleural pressure can exist only when the intrapulmonary pressure is high and can therefore not aid materially in expelling materials from the terminal bronchioles.

Obstructions lower in the bronchial tract were productive of interesting results in some ways. A pea introduced into the bronchus of one lobe and impacted there by means of a contrivance devised by one of the class[2] completely obstructed the flow of air to that lobe. The position of the lobe which later became atelectatic could be recognized by auscultation and percussion and at the autopsy this was verified and the bronchus behind the obstruction found to be filled with a thick mucus. It is more difficult to produce partial obstruction of a bronchus, but it could be done by pushing a piece of rubber tubing into the bronchus by the aid of a device similar to that used with the pea. The results of this experiment are as yet incomplete but it is thought probable that dilatation of the bronchus and the portion of the lung supplied by it may arise behind this obstruction. The measurement and recording of the pressure in the bronchus behind partial and complete obstructions has also been undertaken by members of the class and will be detailed in a separate note. When the lungs are suspended by a tube open to the air in an otherwise tightly corked bottle and the air partly sucked out of the bottle the conditions in the thorax are approached. If now one bronchus be constricted and alternate rarefication and condensation of the air in the bottle carried out (respiration), the free lobes will alternately expand and contract but the constricted lobe will in addition continuously expand, which demonstrates the imprisonment of the inspired air. For this result it is necessary of course that the inspiratory force should be sufficient and that the time allowed for each expiration should not be too long. In many cases bronchiectasis and emphysema of the lungs seem to depend in part upon just such a condition.

It is difficult to produce emphysema in animals—its mechanical principles are included in the above experiments but it seems probable that other changes such as alterations in the elasticity or elastic strength of the lung tissue are necessary factors in the human cases in spite of the negative results which have been obtained by various investigators, who have stained and studied microscopically the elastic tissue in these lungs. Instead of this, one of the class is engaged in determining the elastic coefficient of a series of lungs at autopsy, including cases of emphysema, by measuring the intrapleural tension and then by means of a manometer, the elastic recoil of the lung itself when distended with various definite amounts of air or fluid. These results will also be detailed separately, but already it seems that the elasticity varies enormously in different lungs.

It is well known of course that emphysema is a common result of asthma in which there is supposedly a narrowing of the bronchi with respiratory distress and we have attempted to repeat the experiments of Brodie and Dixon who, recording their results by oncographic methods, succeeded in producing narrowing of the bronchi and consequent limitation in the expansion of the lobe of the lung enclosed on the oncometer, by stimulating the vagus or the nasopharyngeal mucosa. We could, however, in our experiment produce no change in the curve recorded from the lung, possibly because we used chloretone as an anæsthetic in order to avoid the ether or chloro-

[2] The pea was fastened on the point of a pin, the head of which was twisted into a loop into which a long wire was fastened. This was passed through a long glass tube slightly bent and of a caliber so small that the pea could not enter; with the pea thus held against the end of the tube the whole was pushed firmly into the bronchus through a tracheotomy wound and the pin then pulled out by means of the wire, after which the tube was removed.

form which they say destroy the activity of the bronchial muscles, or the nerve endings in those muscles. In this animal the stimulation of the vagi caused pupillary changes and protrusion of the eyeball and the intestinal musculature responded actively, but still it may be that other experiments without general anæsthesia would give positive results in the case of the bronchi also.

As to the distribution of emphysema the statements seem a little exaggerated to fit the theory; it is true that the edges of the lobes are generally more distended than the main body of the lung, but it is not so evident that the emphysema corresponds accurately with the variations in intrapleural and hence intrapulmonary pressure in different regions of the thorax as Tendeloo appears to believe. Nor could we support his theory as to the distribution of fluid in the lung in cases of *drowning*, i. e., that the less mobile portions of the lung receive the fluid while the air is drawn from those alveoli into the actively expanding marginal and peripheral ones. It is true that when an animal was drowned at the end of an experiment by plunging its head under blue gelatin the fluid was found especially in the paravertebral portions of the lungs, and the air in the anterior and marginal portions. But in another animal drowned with the same material, but while lying on its belly, the blue gelatin was found at autopsy almost entirely localized in the ventral and marginal portions of the lung, while the paravertebral parts were pale and air containing. Evidently it is a question of gravitation—the heavy fluid sinks to the lowermost parts of the lungs.

Œdema of the lungs proved as always an interesting and difficult topic. The only easily conceivable cause of general œdema of the lungs suddenly appearing and causing death or again disappearing to reappear sometime later in a bedridden person, is as Dr. Welch has pointed out, a disparity in the activities of the two ventricles such that a *progressively increasing* amount of blood stagnates in the pulmonary circulation. This condition is not produced by a valvular lesion of the heart for there a constant amount of blood stagnates while a decreased amount circulates. Nevertheless it is possible, in spite of the fact that by violent interference œdema can be produced in normal rabbits, that the long standing effects of valvular lesions, chronic passive congestion, etc., may be an important predisposing cause leading to œdema of the lung when the left ventricle finally fails.[3] This is suggested because it is known to be so difficult to produce œdema by mechanical means in the dog. This we attempted by throwing the left ventricle out of function gradually and slowly by making hypodermic injections of strong alcohol into its muscular substance until finally it became almost completely coagulated and stiff, while the right ventricle still contracted actively. In such a case curves taken from the pulmonary vein and the carotid artery showed a marked rise in pressure with strong pulsation in the pulmonary, while that from the carotid sank very low and almost completely lost its pulsation. The left auricle became turgidly distended with blood, but no œdema of the lungs resulted. The same result occurred in a rabbit after the same experiment. On the other hand in the course of some observations of the movements of the heart in another dog, death ensued from the development of a most striking gelatinous œdema of both lungs without any injury having been done to the heart and without any adequate explanation being found. It seems evident that there is still some unexplained factor in the production of pulmonary œdema.

Time did not allow of the detailed study of the relation of the nervous system to the respiratory organs, but it was possible to demonstrate the simple phenomena such as those which arise from the stimulation of various afferent nerves. Rather inconstant and irregular effects followed most of these experiments, but the stoppage of respiration by stimulation of the laryngeal nerves and by the sudden stimulation (in drowning) of the terminals in the pharyngeal and laryngeal mucosa was constant. Sneezing and coughing reflexes were also characteristic and the well known results of vagus stimulation were brought out. Stimulation of the cœliac plexus in our hands brought about stoppage of the respiration but by comparison with the results of others this must be an inconstant phenomenon. The modifications of respiration resulting from dyspnœa, asphyxia, etc., as well as those from hyperventilation are well known. Several efforts were made to demonstrate vasomotor nerves in the lung with the pulsating manometric tracing from the pulmonary vessels as the test object, but the stimulation of all nervous connections failed to give us definite evidence of their existence. The beautiful experiments of Eyster on the production of Cheyne-Stokes respiration by the elevations of intracranial pressure are familiar and are of great value in this connection.

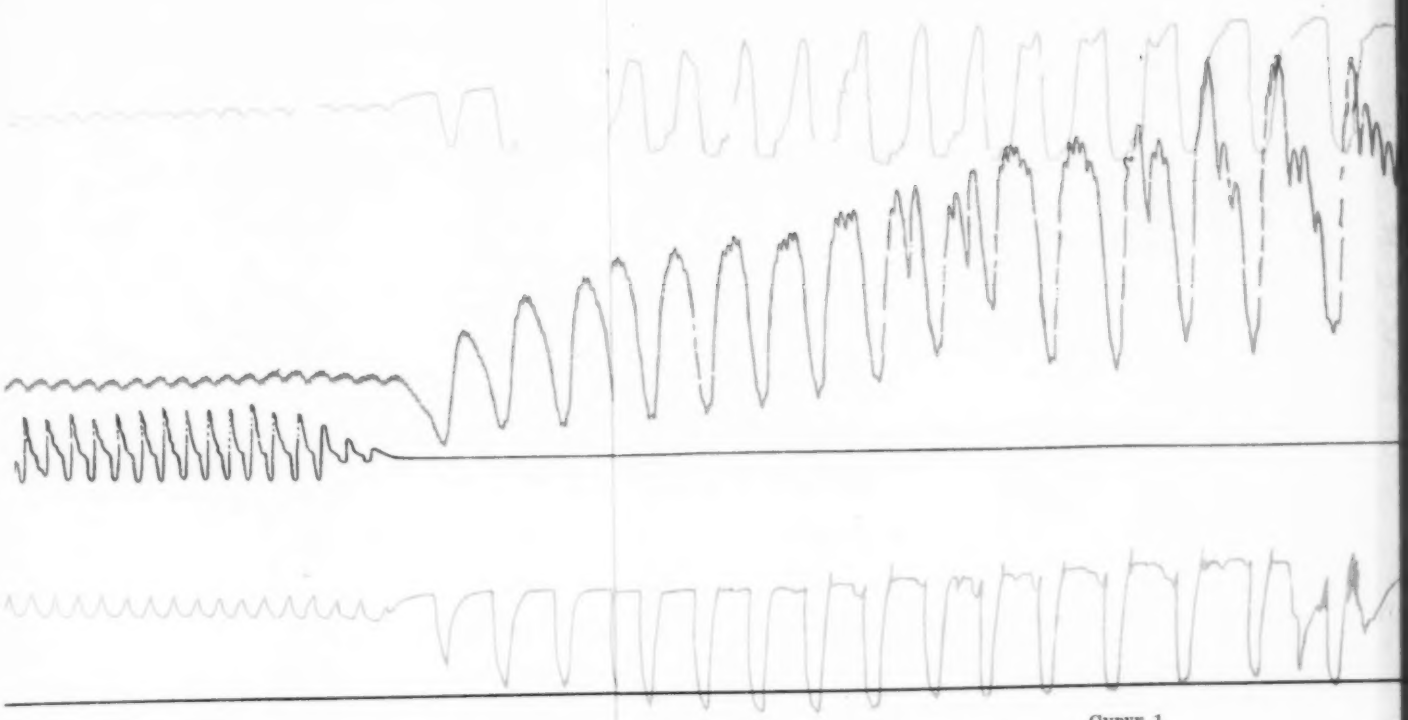
The introduction of foreign materials into the lung by way of the trachea affords an experimental method for the study of pneumonoconiosis, and the injection of emboli into the jugular vein and thus into the heart and pulmonary arteries is instructive in connection with infarct formation, but these as well as the various types of pneumonia and bronchitis may be studied much better in the wards and at autopsy, and therefore little time was devoted to them.

Next year, if opportunity presents itself, the similar experimental study of another group of organs, probably the digestive system, will be taken up.

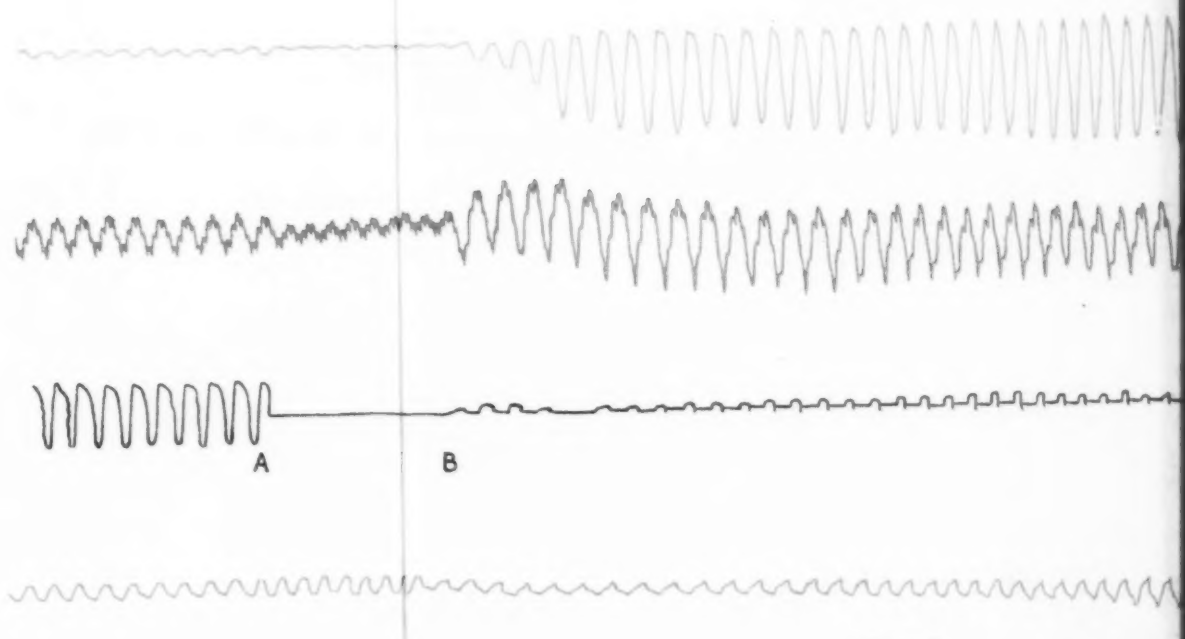
EXPLANATION OF CURVES.

CURVE 1. *Asphyxia with complete obstruction of the trachea.*—The uppermost tracing is from the jugular vein, the canula being nearer to the heart than the first valve in the vein. The second is from the carotid artery, the third from the trachea, the fourth from the thoracic wall (7th rib laterally), while the fifth is the base line.

[3] A case recently seen at autopsy seems to throw some light upon this point. There was advanced stenosis of the mitral valve with consequent chronic passive congestion of the lungs. There had developed within the last few days of life fresh vegetations upon the edges of the old scarred valves, so large as to occlude almost completely the mitral orifice. The patient died with extreme œdema of the lungs. The conditions here seem to correspond almost exactly with those proposed by Dr. Welch.



CURVE 1.



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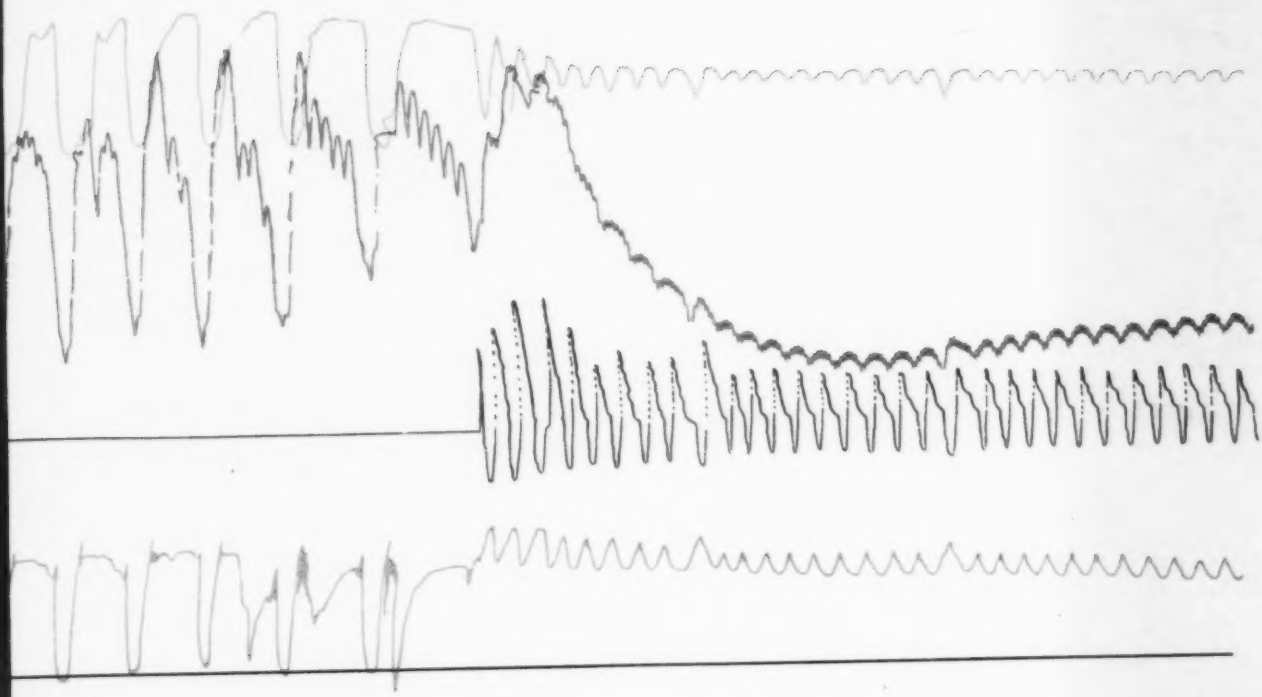

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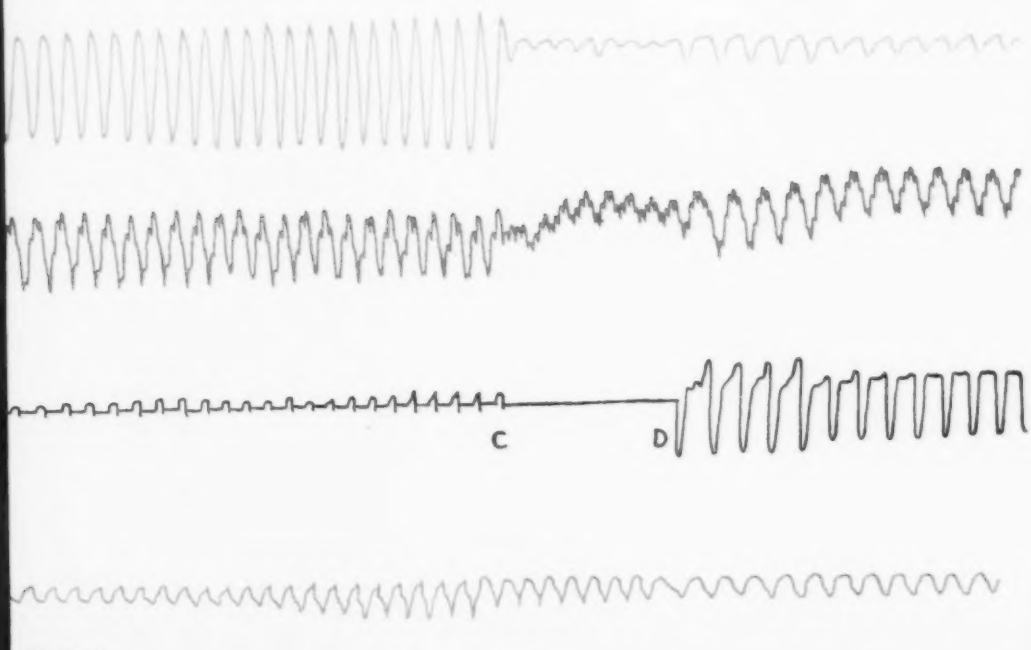
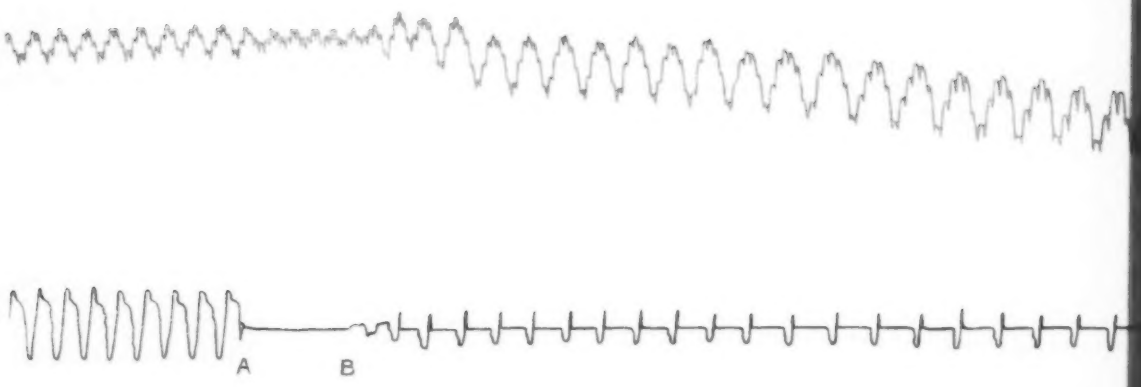
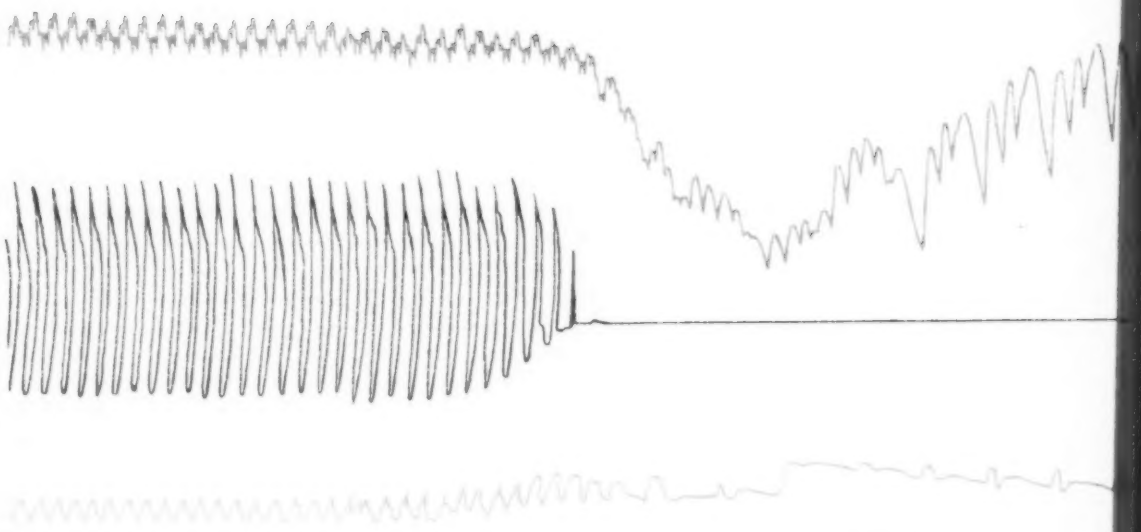


CURVE 2.



CURVE 3.



CURVE 4.

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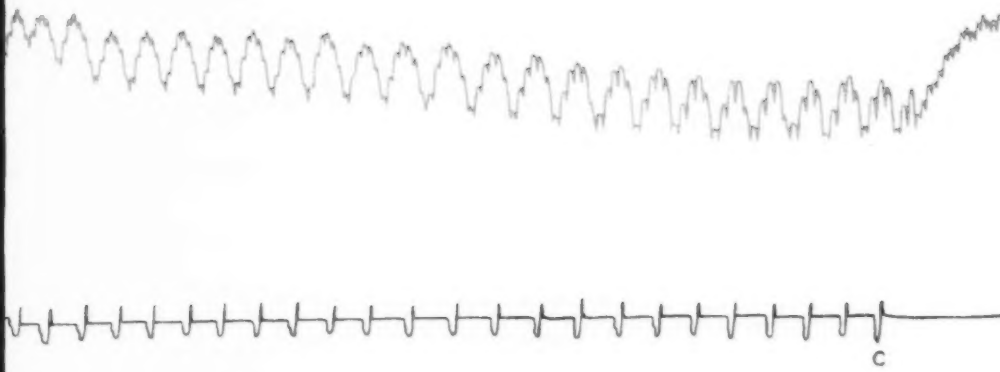
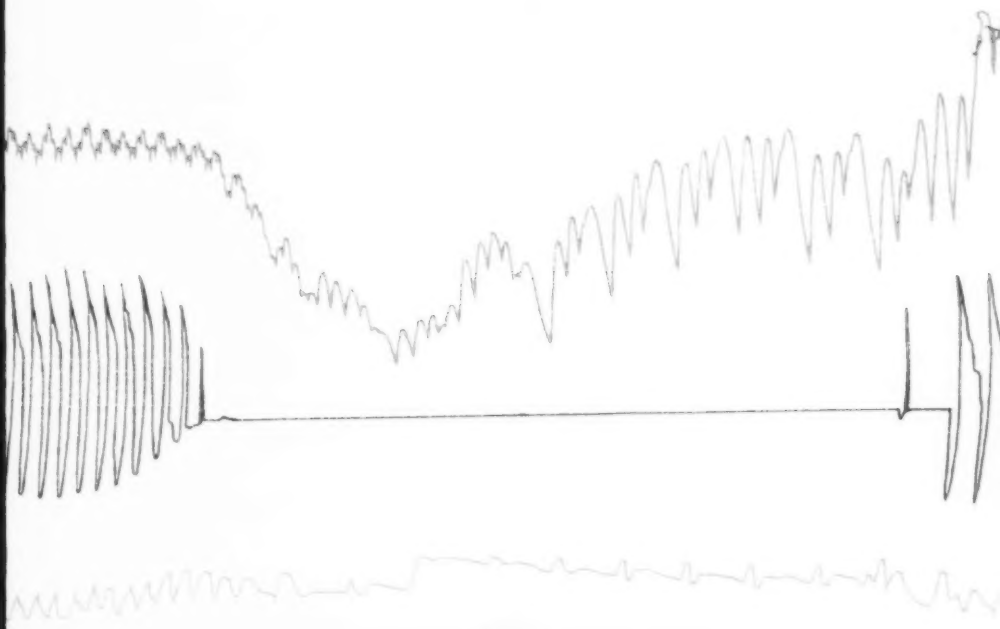
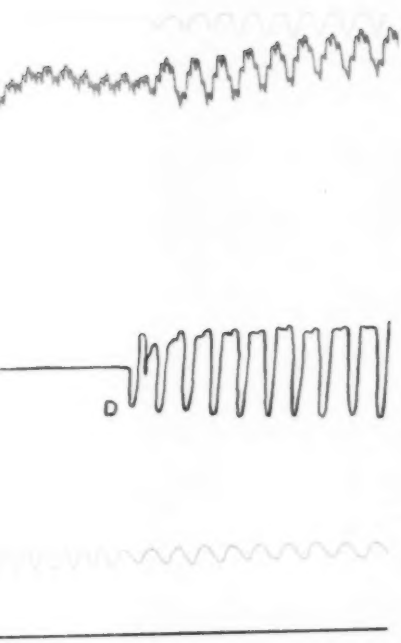


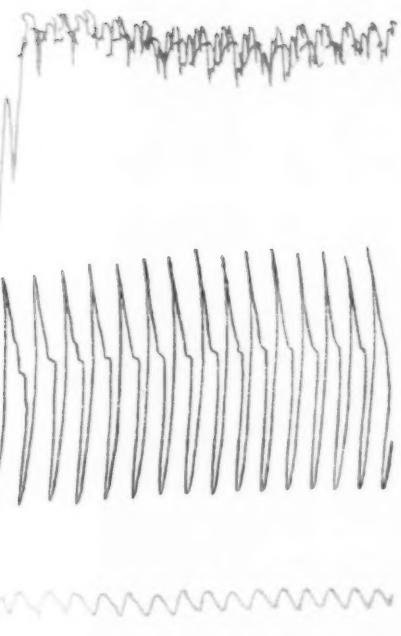
CURVE 3.



CURVE 4.

PLATE VII.





The respiratory record from the trachea ceases when the trachea is obstructed and almost immediately there begin prolonged inspiratory movements of the thorax with corresponding great waves in the arterial and venous blood-pressure. The maximum venous pressure appears a little later than that in the carotid. The pens are precisely superimposed in all the curves.

CURVE 2. *Valvular obstruction of the trachea such that expiration only is possible.*—The recording apparatus constantly produces slight dyspnœa, which is relieved at *AB* and *CD*, while the valve is being inserted. At those portions of the curve the arterial and venous tracings are most nearly normal. The tracings correspond to those in Curve 1. At *B* the valvular obstruction is produced, the lungs gradually empty themselves as far as possible but the respiratory excursions of the thorax increase in amplitude. The change in pressure relations within the thorax produces large waves of arterial and venous pressure.

CURVE 3. *Valvular obstruction in the trachea such that inspiration only is possible.*—The lettering and tracings correspond to those in Curve 2. At *B* the lungs begin to be distended by the imprisonment of air. As in Curve 2 this change in the air-content of the lung is not shown in the tracing. The respiratory movements of the thorax become more and more shallow, owing to the accumulation of air within it. Large waves appear in arterial and venous blood-pressure and the arterial pressure is lowered, while the venous pressure rises, and a condition of cyanosis and venous engorgement ensues.

CURVE 4. *Pneumothorax rapidly produced by forcing air into the pleural cavity.*—The lungs become compressed and blanched and show no further respiratory movements, although violent and prolonged respiratory movements are made by the thorax. The amplitude of these, however, is slight, owing to the permanent distension of the thorax with air. In this respect the condition differs greatly from that seen in closed pneumothorax in the human being, especially in that the dog's thorax forms practically one large cavity. In this case there is marked elevation of venous pressure with large waves corresponding to and following the respiratory movements. The arterial pressure sinks to a low level, but gradually rises with great waves, due to respiratory movements.

RIGHT MESO-JEJUNAL HERNIA.

BY W. G. MACCALLUM, M. D.,
Associate Professor of Pathology,
AND
R. T. MILLER, JR., M. D.,
Resident Surgeon, The Johns Hopkins Hospital, Baltimore.

The admirable book of Moynihan on retroperitoneal hernia renders any detailed discussion of the nature of the fossæ in the upper part of the abdominal cavity unnecessary, but the rarity of the particular type of hernia with which we have met in this region makes our case seem noteworthy.

It is made clear by a number of writers that there occur, with varying frequency, several fossæ about the duodenum and duodeno-jejunal flexure into which under certain circumstances the loops of the small intestine may pass sometimes to such a degree that an enormous sac is formed pushing toward the left but with its orifice facing to the right, capable of containing almost the whole of the small intestine. The particular fossa concerned may often be determined by the relation which the inferior mesenteric vein and the left colic artery bear to the margin of the orifice of the sac. Such herniæ are spoken of by Moynihan as left duodenal herniæ to distinguish them from others which originate near by but in a quite distinct fossa and project toward the right. These are designated by him right duodenal herniæ, although in truth, as will appear later, their relations to the duodenum are by no means so intimate as to suggest this name.

Moynihan in discussing the so-called right duodenal hernia reviews the previous descriptions of fossæ which might receive the loops of intestine and become distended into hernial sacs. In this review of the literature he refers especially to the last paragraph in Waldeyer's paper,[1] which is indeed of great interest so that we may copy his translation here. "Finally, I will refer to the importance of the mesenteric vessels in the raising up of peritoneal folds and the formation of fossæ. Especially is this the case with the superior mesenteric artery, as it arches downwards with slightly concave curve to the right. I have not seldom, in embryos, found a fossa in the mesentery in the concavity of this arch. When the artery is prominent the fossa may be as much as half a centimetre deep, with its closed end directed downwards. I have found this fossa four or five times in fifteen embryos of fifteen to twenty weeks. At a later period it seems to be flattened out. In the adult I have never met such a condition; but it is noteworthy that already many cases of hernia into the mesentery and through "rents" in the same are described, for which, perhaps, this condition may afford an explanation."

Further he refers to the paper by Brösike, who describes the recessus para-jejunalis which Moynihan regards as identical with Waldeyer's fossa. Brösike, in speaking of his case, describes the condition as follows (Moynihan): "In this case the duodenum and the flexura duodeno-jejunalis were normal. From the flexure the jejunum ran obliquely downwards and to the right, adherent to the posterior abdominal wall, and devoid of mesentery. At the level of the fourth lumbar vertebra the mesentery began. On lifting up the first free portion of the jejunum, there could be seen behind and to the right of it a fossa, bounded by a sharp peritoneal fold, which, for want of a better term, I call the 'plica para-jejunalis.' On introducing the finger into the fossa, it could be felt to push

[1] Virchow's Archiv, 1874.

its way between the mesentery and the posterior parietal peritoneum. There was no abnormality anywhere in the peritoneal cavity, but the free mesentery was strikingly long." He especially emphasizes the importance of the adhesion of the jejunum to the posterior abdominal wall in the formation of this fossa, but Moynihan shows that an analysis of the cases proves that this adhesion is not even of frequent occurrence.

From these descriptions it appears that there may occur on the left side of the mesentery at its root near the transverse portion of the duodenum, and hence in the portion subtending the upper portion of the jejunum, a depression or fossa hollowed toward the right and with its wide mouth opening toward the left. This is said to be more distinctly seen in children than in adults. Its anterior border is formed by the superior mesenteric artery, which arches over and in front of it. At its upper margin there may lie the duodenum; behind is the loose tissue forming the actual root of the mesentery. This is by no means so definite a saccular fossa as is commonly seen on the left side of the ascending portion of the duodenum or in the neighborhood of the cæcum but is rather a shallow concavity in the mesentery. If one lift up the loops of small intestine in the normal individual this region is usually found to be perfectly smooth and show no depression, but if the mesentery be viewed by transmitted light looking from right to left it is seen that there is at that point an extremely thin area, sometimes two such areas separated by a thicker band of tissue and sharply bounded anteriorly by the stout superior mesenteric artery with its accompanying veins, etc.

This can hardly be spoken of as a fossa, and indeed if this be the condition normally it is difficult to see by what force the intestinal loops could be pushed through that thin area. Evidently in all cases of hernia at this point there must be some disturbance which would give a chance for the bulging in of the intestines, possibly in the form of a rent in one leaflet of the mesentery which later develops into a fossa, possibly in some congenital laxity of this portion of the mesentery.

In all the cases described the sac bulges into the loose tissue behind the posterior parietal peritoneum, *i. e.*, stripping up in some cases the left leaflet of the meso-colon of the ascending colon, when it comes to lie mesial to the ascending colon; in other cases passing behind that portion of the intestine and stripping up the right or outer leaflet of the potential meso-colon so that the sac comes then to lie as in Brösike's case to the outer side of the ascending colon.

It seems quite possible, however, that instead of thus burrowing behind the posterior peritoneum the fossa might consist merely of a bulging of both layers of the meso-jejunum toward the right so that when the sac is complete it lies within, *i. e.*, mesial to the ascending colon, its walls or coverings being formed not of one layer of the meso-jejunum and one layer of posterior or parietal peritoneum but simply of the two layers of the meso-jejunum. Indeed, this seems to be what has actually happened in the case which we wish to report, as follows:

Case History J. G. Surgical No. 21,454. Colored, aged 41. Admitted October 19, 1907, complaining of abdominal pain and constipation. Immediate laparotomy. Findings: Incarcerated internal hernia. Reduction of hernia. Closure. Death in 28 hours, apparently due to acute cardiac dilatation.

Patient was admitted with the following history: Up to onset of present illness he had always been well. No history of previous attack.

Present Illness.—Onset one week ago, October 12, 1907, with acute crampy abdominal pain below the umbilicus, more marked on the left side. The pain has been almost constant since onset but there have been exacerbations. He first vomited October 15, the vomitus being thin, sour, and yellowish, but not fæcal; since then he has vomited once a day. His bowels moved slightly October 14, but have not moved since, in spite of moderate catharsis. There has been no pain on micturition. He has had morphia twice in the past 24 hours, ¼ gr. each time, and some previously.

Physical Examination.—Pulse 76 to the minute. Temp. (per rectum) 99.4°. Facial expression calm. Pupils contracted. Tongue soated with yellow fur. Abdomen markedly distended, the distension being more marked below level of umbilicus; distension equal on two sides. Abdomen moves very slightly with respiration, less in lower half than elsewhere. Intestinal loops plain but no visible peristalsis. Abdomen fairly soft, in spite of distension. Tenderness only slight and most marked in left lower quadrant. Abdomen is tympanitic as far as flanks, where there is about one finger's breadth of movable dulness. Liver pushed well up reaching 8 cm. from costal margin in right mammillary line. Rectal examination negative.

Note on Chest.—Expansion good. Percussion negative. Auscultation: "cogwheel" type of respiration. Heart: Systolic murmur at apex, not well transmitted to axilla. Other sounds clear. Area of cardiac dulness not enlarged.

Gastric Lavage.—Stomach washed out as a preliminary to the administration of ether. Over 1½ litres of a turbid, yellowish fluid obtained, very foul, but not stercoraceous.

Patient was evidently suffering from an acute intestinal obstruction from some undetermined cause and an immediate laparotomy was advised and performed. Patient had been given considerable morphia before admission, which complicated the anæsthesia to a certain degree.

Operation.—October 19, 1907. Ether anæsthesia.

Exploratory laparotomy for acute intestinal obstruction. Findings: Incarcerated internal hernia. Liberation of the hernial contents. No gangrene of bowel. Closure of sac.

A right rectus incision was made and the peritoneum opened, allowing the escape of a small amount of clear yellow serous fluid. Loops of bowel protruded into the wound; these were carefully packed off with Mikulicz pads and an exploration made. Lying exactly in the central portion of the pelvis directly between the rectum and the bladder was found a globular mass which was possibly 12-15 cm. in diameter, somewhat pear-shaped, with the small end upward. This mass was lying quite free within the peritoneal cavity, no adhesions about it at any point. It resembled at first touch a very much distended bladder but the patient had been previously catheterized and this was out of the question. A hard fibrous band was found running downward from the region of the epigastrium on the right side and into this mass. The mass was dislocated upward into the wound and was found to be a bunch of markedly distended small intestines lying within a hernial sac which was covered on both sides with peritoneum; the sac wall was extremely thin, about the thickness of tissue paper, and through its walls could be seen coursing a moderate number of veins of very small calibre. The condition was then recognized as being an internal hernia and attempt was made to reduce the contents of the sac. It was found easily pos-

The illustration shows the sac (*b*) as it appeared at the autopsy, its large mouth being represented at (*a*). The dotted line (*c*) is meant to represent approximately the outline of the hernial sac, as it appeared at operation. The para-jejunal fossa is clearly shown and to its left, at (*d*), the two blood-vessels cross each other to form the arch described in the text.

sible to dislocate these loops of bowel inward towards the mid line; that is, the mouth of the hernia sac pointed towards the mid line, the sac lying to the right-hand side. The sac was then turned inside out and loosely stitched in this position by transfixing sutures of fine black silk taken at the base of the sac. The contents of the sac were slightly adherent by old tough adhesions which were not divided as they were evidently not causing the acute obstruction. The intestines seemed in very good condition; there was no evidence of gangrene at any point, and the cause of the obstruction having been relieved, the wound was closed.

Post-operative Notes.—Upon return to the ward patient's respirations were only five to the minute and very shallow; pulse was 120. Patient was given a subcutaneous infusion of 1000 cc. of salt solution and his condition improved somewhat.

Leucocyte count four hours after operation, 8,400; 20 hours after operation, 11,000.

October 20.—Patient after operation complained of some pain in lower abdomen and was rather restless. Vomited several times after operation. At 1 a. m. his stomach was washed out and a quantity of yellow fluid obtained. Patient's bowels moved during the night. There was considerable distension over upper portion of the abdomen. Toward evening he complained of shortness of breath and his pulse was rapid and weak. When seen at 9 a. m. to-day, patient lay in bed, restless, with anxious expression and gasping for breath. Pulse rapid, 145 per minute (reached 160 at 8 a. m.) and weak. Examination of chest: Respirations labored; percussion negative; auscultation revealed a "cogwheel" type of respiration; a few râles toward right base, but otherwise negative.

Heart.—Deep cardiac dulness not increased. There is a definite systolic murmur over the apex which accompanies first sound; not well transmitted to axilla. Second sound clear. Pulmonic slightly accentuated.

Abdomen.—Much distended, especially upper half. Gastric lavage done and a large amount of yellowish mal-odorous fluid obtained. Patient given an infusion and stimulated with strychnine. He responded fairly well but gradually sank during the day and died at 7.25 p. m. The air hunger persisted all day.

Résumé.—Patient's bowels moved nine times between operation and his death. There was practically no abdominal tenderness and, except for the slight distension of his abdomen, there was no evidence of an intraperitoneal complication. Patient's pulse after operation increased steadily in rate, becoming progressively weaker, more thready and finally running; examination shortly before death seemed to show a moderate cardiac dilatation. Patient presented clinically the appearance of a cardiac collapse with loss of compensation.

Autopsy performed next day, No. 2950, was as follows:

Anatomical Diagnosis.—Hernia through the root of the mesentery, with strangulation; bronchopneumonia.

The peritoneal cavity was found to contain a small amount of blood-stained fluid, and the intestinal coils were slightly adherent to one another. They are extraordinarily distended, the upper coils of the ileum completely hiding the transverse colon. No definite obstruction was found. The mesentery of the jejunum is extremely lax and has been drawn up and sutured together so that no sac is actually visible. When these sutures are removed however the distensibility of the mesentery is such that almost the whole of the small intestine can be replaced in the sac. The adhesions formed about the mesentery of that part which was invaginated in this sac have been torn through.

The intestines were injected through the mesenteric artery with red gelatin and subsequently dissected. It is found that there is a very distinct para-jejunal fossa lying above the jejunum. This has a thick margin which extends over to the duodeno-jejunal flexure. The cord-like margin of the fold contains a band of muscle which can be frayed apart. This turns downward along the middle of the sac and runs to form the edge of a loose fold which might have bounded the superior duodenal fossa. There is a sac there which is more or less continuous with the main sac about to be described. In the communication between these two the inferior duodenal fossa is quite lost. The arteria-colica sinistra starts upward at about 2 cm. to the left of the lower margin of the para-jejunal fossa. It forms an arch in the meso-colon with the mesenteric vein, but the arch lies nowhere near the orifice of the large sac. Indeed, it is somewhat distant from the para-jejunal fossa, in the formation of which it plays no part. The relationship of this arch to the duodenal fossæ is in general not so definite as is described in literature. The duodenum is normal in its position. The jejunum is quite free and has a long mesentery. At its root the tissue becomes extremely loose and wrinkled and the peritoneum covering the duodeno-jejunal flexure suddenly assumes this same character and is continuous with the lining of the very large sac which projects through the mesentery of the jejunum toward the right. The mesentery of the jejunum is quite compact down to the main branch of the superior mesenteric artery which runs in it; that is, the branch which gives off anteriorly so many smaller branches to the mesentery, and which is accompanied by a large vein. Underneath this branch, which forms an arch, both leaflets of the mesentery become extraordinarily lax and are distended into a large sac which at the time of the operation projected far down toward the pelvis on the right side. It is thus seen that this sac is not made up by the burrowing of a stretched leaflet of the mesentery underneath and behind the posterior peritoneum as is usual, but is constituted simply by a distension of the two leaflets of the mesentery and therefore appears mesial to the ascending colon. The outer leaflet of the sac is continuous on the right with the posterior peritoneum running over to the ascending colon, and this is also extremely lax. The condition may therefore be regarded as a meso-jejunal hernia, although it is true that the duodenal fossæ are more or less involved in the sac and can no longer be clearly discerned as such.

ABNORMALITIES OF THE PULMONARY BLOOD-VESSELS.

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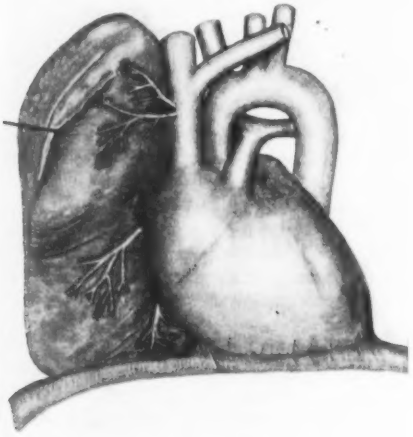
(*From the Pathological Laboratory.*)

As, after searching the literature for cases of abnormal pulmonary circulation, no cases were found, it seems of sufficient interest to report briefly two such cases.

The first case (Path. Museum, No. 1669) was obtained originally from the anatomical laboratory. The specimen consists of the heart and lungs of a child evidently about two years of age. The heart, which is dilated and hardened in situ, seems normal in every other respect. The large vessels

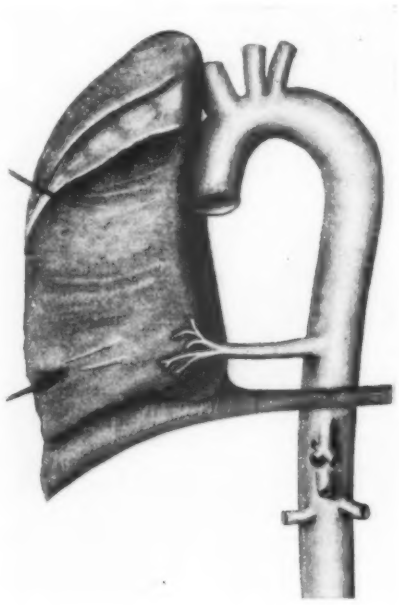
which enter and spring from the heart are normally situated. The pulmonary artery arises from the right ventricle and extends backward, to the left of the ascending aorta for a distance of about 2 cm., where beneath the arch of the aorta it divides into a right and left branch. The right branch bends very sharply to the right and, passing above the pulmonary veins, crosses the right bronchus and gives off two medium-sized branches which supply the upper lobe of the right lung. Two branches are then given to the middle lobe, and the artery ends in three branches to the lower lobe. The left branch of the pulmonary artery supplies the upper and lower lobes of the left lung with an equal number of branches. The left pulmonary veins arise in a normal manner from the upper and lower lobes of the left lung and run directly and separately to the left auricle, into which they empty. The veins from the middle and lower lobes of the right lung run directly and separately toward the right aspect of the left



auricle, and joining just before the auricle is reached, enter it as one large vessel. The striking abnormality present in this case is seen in the fate of the arterial blood from the upper lobe of the right lung. Arterial blood from this lobe is collected by numerous branches which join to form two larger vessels, which, in turn, converge toward the middle line of the body and very close together enter the superior vena cava at a point about 1.5 cm. above its point of entrance into the right auricle.

In the second case (Autopsy No. 2949), that of a white male, 80 years of age, the anatomical diagnosis was: Bronchopneumonia, chronic diffuse nephritis, arterio-sclerosis, thrombosis of middle cerebral artery, encephalomalacia, inguinal hernia, and anomalous pulmonary artery from aorta.

No abnormalities were noted in the structure or blood-supply of the left lung. An interesting coincidence in this case is that the right lung is incompletely divided into two lobes by a short shallow fissure which is situated about midway between the apex and the base and runs from the postero-lateral aspect obliquely forward for a distance of about 15 cm., and disappears upon the anterior surface. Upon removal of the right lung, a hard calcareous body was encountered upon the mesial aspect near the base. This is found to be an artery arising from the aorta at a point about 5 cm. above the diaphragm, and running directly over into the lower mesial portion of the lung. Here it breaks up into six large short branches which end quickly. These branches are distributed to an area of lung about 3 cm. in diameter. The artery is about 6 cm. in length and about 8 mm. in diameter. The lumen is completely obliterated from its origin to the point where it branches, by a firm gray thrombus. The walls of the artery and its branches are very thick and contain a large deposit of calcium salts. Since the thrombus appears to be very old, and the lung tissue in the area to which the small



branches are distributed is air-containing and appears normal, and since there is an extensive obliterating endarteritis in the small branches, it is very evident that the extra blood-supply to the lower portion of the lung was entirely superfluous.

In pig embryos 5 mm. long Flint [1] says that the pulmonary vein develops from the undivided portion of the sinus venosus at the level of the pulmonary anlage, and that as the stem bronchi increase in size, right and left pulmonary veins develop from the capillary plexus which surrounds them. These are formed upon the opposite side of the bronchus from the arterial capillaries. Thoma found in the chick that the arteries and veins are originally simple capillaries. Their growth in size bears a definite relationship to the velocity of the blood stream in them, while their arterial or venous nature is determined by the character of that current, a high pulsating column of blood giving rise to an artery, while a low-

[1] J. M. Flint. American Journal of Anatomy, Vol. VI, 1906.

pressure constant current would be the determining factor in the formation of a vein. The nature of the current would be dependent upon the position of a given capillary, whether it be upon the arterial or venous side of the capillary plexus. As to the cause of vascular development there is some dispute, Thoma believing that new growth of vessels is due to a rise in blood pressure in the vascular area, while Flint thinks that new growth of cells is the primary stimulus for the production of new capillaries. It seems very probable that both of these factors may play a part in vascular development.

In the first case above described, the abnormality has evidently occurred very early in embryonic life, probably just after the time of the vascularization of the eparterial bronchus. The venous character of the vessels in this case (*i. e.*, carrying blood away from the lung) was earlier determined, but the capillary buds, instead of passing like those from the middle and lower lobes to form a right pulmonary vein, have taken an abnormal course, entering the superior vena cava, mixing arterial with venous blood, thus causing more or less of a vicious circle.

In the second case no explanation can be offered, other than that the vessel described is an abnormal supernumerary one, which can bear no relation to the bronchial arches. Here the branches of the artery bear no relationship to the bronchi, and the area supplied by the artery at the time it carried blood was drained by the pulmonary veins.

TUBERCULOSIS OF THE STOMACH; TUBERCULOUS CAVITIES OF THE LIVER; WITH REPORT OF A CASE.

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(*From the Pathological Laboratory.*)

This case is of interest on account of the localization of the tuberculous process, the extensive involvement of organs rarely affected by the disease, and finally for the possible light it may throw upon the etiology of the process in these organs.

F. B. Colored, female, æt. 20 years. Died December 7, 1907, 7.30 p. m. Autopsy December 8, 11 a. m.

Anatomical Diagnosis.

Broncho-pneumonia; tuberculous bronchial, anterior-mediastinal, and mesenteric lymphadenitis; tuberculous pleuritis; tuberculosis of the lesser peritoneal cavity with extensive adhesions between the liver and diaphragm, liver and stomach, stomach and pancreas; tuberculous cavities in the liver; tuberculous ulceration of the stomach; tuberculosis of the spleen; epithelial necrosis of the kidneys; fatty degeneration of the myocardium.

Body.—Is that of a fairly well-nourished negress, 145 cm. in length. The abdomen is slightly distended. The abdominal fat is well preserved. The peritoneal cavity contains a small amount, (200 cc.) of yellow fluid, in which a few flakes of fibrin are seen. The surface of the peritoneum, over the right rectus muscle, shows several small black shot-like nodules, 2.5 mm. in diameter. The meso-colon is studded, especially near the greater curvature of the stomach, with enlarged yellow opaque nodules from 2 mm. to 2 cm. in diameter. These vary in consistency, some are firm, while others are semi-fluctuant and expel on incision a yellowish, opaque, viscid fluid. The lesser peritoneal cavity is obliterated. The liver is bound down firmly to the diaphragm, the stomach is closely bound to the posterior surface of the liver, and the pancreas to the posterior surface of the stomach. The spleen likewise is adherent to the diaphragm, and parietal wall. The mesenteric lymph glands are large and on section no glandular substance is to be seen, but in its place a yellowish caseous mass. On removing the sternum a large amount of greenish yellow, viscid material exudes from the right side. This comes from a circumscribed, necrotic mass in the right pleural cavity, measuring 3 x 4 x 5 cm. (apparently broken-down lymph glands). Its base is formed by the diaphragm while laterally and posteriorly it is covered by a much-thickened pleura. Its walls are ragged and show a yellowish cheesy surface. Running up from this area a number of enlarged caseous lymph glands are found in the anterior mediastinum. The pleural cavities are partly obliterated by old fibrous adhesions.

Lungs.—The *left lung* is bound down firmly to the parietal pleura by numerous fibrous bands which bleed slightly on division. Here and there, over the roughened surface a few opaque yellowish nodules can be seen. The lung is voluminous, of a pinkish gray color, mottled everywhere by large irregular deep maroon areas. These are non-air containing. The glands at the hilum are not markedly enlarged. Several, however, show on section yellow opaque nodules in the black pulp. The bronchi exude considerable brownish frothy fluid. Their mucosa is reddened. On section the lung tissue is moist, of a pink color, and shows many irregular more congested areas which stand out above the surrounding tissue and have a finely granular surface. These are non-air containing. The *right lung* is likewise bound down by numerous semi-opaque adhesions. Its lower anterior surface is covered by the mass of broken-down lymph glands above described. Otherwise it resembles the left in every respect.

Spleen.—Is small, hard, and firmly bound down to the parietal wall. Its surface is covered by fibrous tags and shows several yellowish, opaque masses; the largest 2½ cm. in diameter. Throughout nodules 2 to 5 mm. in width, similar to the one described on the surface are found.

Note.—On account of the dense adhesions, the diaphragm, liver, stomach, duodenum, and pancreas were removed en masse.

Liver.—The dome of the liver is united to the under surface of the diaphragm, by a dense caseous mass, varying from ½ to 1 cm. in thickness. On its under surface the liver is bound closely to the anterior wall of the stomach, and on attempting to separate them the wall of the stomach is easily torn. On section the liver substance is of a pale grayish-brown color. It is studded, more especially in the portal areas, by opaque grayish-yellow nodules. Several of these show minute green centers. Several cavities are seen; two measuring ½ cm. in diameter, while a third is the size of a pigeon's egg, lying in the posterior portion of the right lobe. These contain a viscid creamy material which when evacuated leaves a ragged wall studded with yellow and green bile salts.

The *gall bladder* is likewise closely surrounded by fibrous adhesions. Its walls are thickened and show numerous tubercles over its surface. It is difficult to force bile through the common duct into the duodenum. The mucosa of the gall bladder shows numerous erosions with undermined necrotic edges. The common duct is patent and empties about 1½ cm. below the pancreatic duct into the duodenum. It is joined by a small duct from the head of the pancreas.

Pancreas.—Is adherent to the posterior wall of the stomach by a dense caseous mass. On section it shows no gross lesion; its ducts are patent.

Stomach.—Is small and as above described closely adherent to the liver and pancreas. The serous surface is roughened by opaque yellow nodules, from 2 to 5 mm. in width. Where it is bound to the liver, it is very friable, tearing readily. The stomach opened along the lower third of the anterior wall, contains a small amount of tenacious, grayish mucus. When this is removed, two extensively ulcerated areas, the one corresponding to the external adhesion with the liver, the other to those with the pancreas, are disclosed. The ulcers show a granular necrotic base on which opaque yellow nodules can be seen. The walls of these ulcers are greatly undermined so that in many places a blunt instrument readily passes beneath the bridges of mucous membrane and allows it to be lifted up as a lattice-work. On section through the stomach wall, it is seen to be markedly thickened. The sub-mucosa shows many yellow nodules which extend to the muscularis and even to the serosa. The mucosa is often intact over such a nodule, but in areas shows the ragged ulceration above described. The stomach wall, along both the lesser and greater curvatures, is pale and of a yellow color. The rugæ are still present. Here and there, a slight nodular area is seen which, on section, reveals a sub-mucous caseous mass. The cardiac orifice is small but the mucosa seems normal. The same is true of the pylorus.

Duodenum.—Is slightly narrowed by the projection of the œdematous villi. Its mucosa is congested, but otherwise it seems quite normal.

Intestine.—In the lower ileum and cæcum, several grayish opaque slightly elevated nodules, about 5 mm. in diameter, are seen. Otherwise nothing of note is to be made out.

Microscopical Notes.

Lungs.—The pleura is thickened markedly by a loose fibrous coat, throughout which many engorged blood vesels are seen. Toward the periphery, where the pleura was in contact with the broken-down lymph glands, there is a dense necrotic mass infiltrated with cells mostly of the polymorphonuclear type.

The alveoli are filled in patches by an exudate of serum, blood cells, mostly polymorphonuclear, fibrin, and a few desquamated epithelial cells. These are all well preserved. The bronchi are likewise filled with exudate.

Spleen.—The capsule is thickened. Typical conglomerate tubercles are found throughout the pulp.

Pancreas.—Except for a marked fibrous thickening attaching it to the stomach wall, it is apparently quite normal.

Stomach.—Shows in many areas, no sign of any tuberculous lesion. Here the mucosa is slightly infiltrated with fibrous tissue and there is a loss of its glandular elements especially in its outer half. There is no marked increase in either the number or size of the solitary follicles. The serosa shows areas of round cell accumulation and not infrequently epithelioid cells can be made out. In places streaks of similar cells come up through the muscularis forming nodules in the sub-mucosa like those on the serosa. Nodules as large as ½ cm. in diameter occur in the sub-mucosa, covered by intact mucous membrane. These are caseous degenerations surrounded by rounds cells and epithelioid cells, and often typical miliary or conglomerate tubercles occur. The muscularis and the muscularis mucosa may be intact about such a mass. Sometimes the muscularis is involved in the tuberculous degeneration and in the majority of instances, caseous areas are found on the serosa beneath the nodules. In fact the most extensive change in the mucosa and sub-mucosa occurs where the stomach is bound to the liver or pancreas, so that in a section one has first liver or pancreas, then exudate and then stomach. Where the mucosa is involved one sees ulcerations of varying sizes. The most typical ones are quite small with deeply undermined edges. The cavity itself being about the size of the nodules above described in the sub-mucosa. These seem as though they may have formed in the solitary lymph follicles. The base of the ulcers is lined by a caseous mass and the edges show many tubercles in various stages of formation. Often several smaller ulcers become confluent burrowing through the sub-mucosa and leaving the partially degenerated mucosa lying free over the necrotic base. Here and there giant cells and tubercles also occur.

Œsophagus.—The œsophagus shows an intact mucosa. The sub-mucosa, however, shows accumulations of round cells, but no coagulative necrosis. (This section was taken just at the transition of the pavement epithelium of the œsophagus to the glandular epithelium of the stomach.)

Duodenum.—Section of the duodenum, just below the pylorus, shows it to be quite free of any of the changes above described in the stomach.

Liver.—The liver is studded throughout with areas of degeneration and cellular infiltration. These are by far most prominent around the bile ducts. Everywhere one sees a granular exudate lying free in the lumen of the ducts. The epithelium is desquamated to a great extent, sometimes stripped off in entire sheets. Surrounding the bile ducts various types of change occur; in some places dense fibrous tissue forms a thick wall enclosing usually, besides the bile duct, also the vessels in the portal spaces; in others the fibrous tissue is not so dense and there are numerous round cells seen throughout it; in still others there is just an accumulation of round cells and epithelioid cells around the small bile duct. These latter often appear as so-called "pseudo-giant" cells. In other areas cavities of varying size can be seen lined by caseous degenerated walls and fibrous tissue surrounding them. In these cavities one finds constantly the remains of the duct epithelium, in long desquamated strands, and bile pigment. In tracing some of these cavities through serial sections, the larger ones do not connect directly with one large duct; however, numerous smaller ducts can be seen to be involved in the degenerative process and to gradually enter the cavity. One small cavity was found, which apparently arose from a single duct. Its epithelium, though desquamated, could be seen lying in one large sheet at the periphery of the cavity. (This same appearance was found in two other cases of miliary cavity formation in tuberculous livers.) A section of the common bile duct, close to where it empties into the duodenum, shows it denuded of its epithelium and numerous areas of round-cell accumulation occur in its wall. The liver tissue, between the areas of degeneration above described, is markedly congested, and shows in a few areas both miliary and conglomerate tubercles, but these are not abundant and rarely attain any great size.

The genito-urinary tract is entirely free of tuberculosis.

Tubercle bacilli.—After repeated efforts a few tubercle bacilli were found in both the gastric sub-mucosa and in the liver.

Although it is impossible to say where the primary portal of entry in this case was the involvement of the tracheal, bronchial and anterior mediastinal lymph glands with the chronic pleuritis seems to point to the upper air passages and the lymphatic system as the path. The diaphragm was probably invaded from the anterior mediastinum, and the ser-

ous surface of the liver, stomach, spleen, and peri-pancreatic tissues were involved by direct extension. That the stomach was involved from without, seems certain. As to the origin of the cavities in the liver, we have the involvement of the gall-bladder and bile ducts in favor of an ascending infection. It seems impossible, however, to rule out the lymphatics which may have carried the process from the peri-hepatic tissue. Strength is added to the last theory when we recall that the large cavity was situated in the posterior portion of the right lobe and at its nearest point was hardly 2 cm. away from the caseous capsule.

It will be of interest to note that among the cases of tuberculous cavities reported, many have been associated with a peri-hepatitis.

Tuberculosis of the Stomach.

Tuberculosis of the stomach is a rare occurrence. Simmonds in 1900, said "No case of *primary* tuberculosis of the stomach has ever come to autopsy." Glaubitt, in 47 cases, found two or more organs, besides the stomach affected in every case; the lungs were affected every time. Ruge, in a recent paper, reviews those cases where with a gastric tuberculosis, the lungs were uninvolved: (1) Hattute: case of miliary tuberculosis of the peritoneum, bronchial and mesenteric lymph glands; chronic pleuritis. (2) Kansow: extensive peritonitis. (3), (4) Petruschsky: diagnosed clinically (no autopsy). (5) Cazin: peritonitis, ulceration of larynx and involvement of bronchial glands. (6) His own case, where there was an extensive peri-hepatitis and peri-splenitis with a chronic pleuritis and peritonitis and ulcerative enteritis. He thinks his case one of primary tuberculosis of the stomach. Fisher De Foy, in 1906, adds another case; the stomach was bound to the liver in several areas by caseous glands, and the lungs were involved. He considered the stomach to be the primary focus. The analogy between these cases and the one reported, is rather striking, and even though it seems that these cases might be of primary gastric origin, the evidence is quite strong in favor of infection of the stomach from without, as will be shown. Van Wart, in 1903, reported a case where there was a caseous mass 3.5 cm. in diameter lying between the two muscular coats of the stomach and covered by a perfectly intact mucosa. There was no other tuberculosis in the body. He thought this lesion probably primary, but it is difficult to see just how the organisms could enter in such a position without leaving some visible trace. If it was due to ingestion of tuberculous material, one would expect to find some involvement of the lymphatics draining the upper alimentary tract, especially the submaxilliary and the sublingual glands, as Orth found in all the animals fed on tuberculous tissue. In his experiments, he rarely found any gastric lesion; occasionally there was a slight hæmorrhagic erosion, and still more rarely ulcers of tuberculous character. This seems to show that primary tuberculosis of the stomach is possible at least in animals.

Secondary involvement of the stomach is of much more frequent occurrence. Hamilton, in 1897, collected the cases in the literature, and added three cases. In 1898, Blumer was able to collect 30 authentic cases, to which he added one. Glaubitt, in 1901, reported 47 cases. The cases reported since then likewise are few. Ruge, Fisher DeFoy, Curschmann, Van Wart, Alexander, Kansow, Rosset, Cone, Reinhold (and a few others whose work has been inaccessible to me), reporting each one case. The rarity of the lesion is self-evident when we recall that Simmonds only found eight cases of gastric involvement in 2000 autopsies on tuberculous patients.

To what does the stomach owe its immunity? (1) It was thought that the secretions of the stomach had some deleterious effect upon the organism, but it has been shown by Faulk and Frank that organisms suspended in gastric secretion and incubated at 38° for six hours were unaffected and only lost their virulence after 24 hours. (2) Simmonds thinks the essential point is whether the active organism can harm the mucosa which is secreting normally. He reports a case where cancer and tuberculosis existed side by side, and thinks, the carcinoma was primary, that it led to a change in the gastric juice which allowed the tuberculous process to develop. He mentions that there was pyloric stenosis. The motility must have been affected as also the length of time ingested material remained in the stomach. These two latter factors together with the thinned wall of the dilated organ are important factors in the development of the lesion. (3) Dürck and Oberndorf, and Curschmann consider motility as one of the most important protective agencies. (4) Struppler thinks intact epithelium the best protection against ingested tubercle bacilli, but that they may affect the lymph follicles without damaging the epithelium. Later, in the discussion of tuberculous cavities in the liver, we shall have occasion to speak of this again; it is the same question that arises in tuberculosis of every organ. Can any organism (which is not motile) pass through epithelium without leaving any sign? But be that as it may, certainly if there is a lesion, due to a small loss of substance, consequent upon an ecchymosis, as Hamilton suggests, it is easy to conceive of this as a favorable place for any organism to center and develop. (5) It is said that the sparsity and depth of the lymphoid follicles is against the occurrence of tuberculosis of the stomach. Barbacci considers them the primary seat of infection. Przewoski likewise considers them of importance. He describes several cases, complicated by chronic pulmonary phthisis, and thinks the duration of the pulmonary involvement an important factor, since the physiological activity of the stomach is often lessened, and because there may be some predisposing pathological change such as catarrhal inflammation. Whether these changes are sufficient to alter any antiseptic action of the gastric juice seems doubtful, as Marfan and Schwalbe have shown many cases of pulmonary phthisis to be suffering from chronic gastritis without any tuberculous involvement supervening. Dobrowolski has lately shown that the lymph follicles which are not always so rare in the human stomach are markedly increased in catarrhal gastritis, so much so in fact, that he has applied the name "gastritis granulosa" to this change. It is of interest to note here a case recently reported by Cone where

the stomach was the seat of a diffuse chronic gastritis in which there were nodules of several histological types; among these, nodules specifically tuberculous confined to the lymphoid follicles. On the other hand, Wilms thinks the lymph follicles have nothing to do with tuberculosis. He reports a case of numerous tubercles in the sub-mucosa of the stomach of a child nine months old, dead of generalized tuberculosis. He thinks in a child of this age the lymph follicles must be scanty and still in his case there was marked tuberculous change. (6) Przewoski also suggests the nature of the organism may have much to do with the lesion. All these factors taken into consideration seem to be evidence enough for the rare occurrence of infection through the gastric mucosa.

A more common mode of infection is thought by Barbacci to be through the blood or lymph stream. Simmonds says, "Contrary to the formation of ulcers, the finding of miliary tubercles of hæmatogenous origin, is not rare." He has found these in several cases. Wilms and Kaufmann have also recognized this mode of infection and they think tubercles will be found in these cases according to the care with which one looks for them.

The last mode of infection to be considered was first emphasized by the cases of Birch-Hirschfeld and Hattute. In these there was a pre-existing inflammation of the serosa which had spread to the mucosa by direct extension. In many of the other reported cases, there exists a circumscribed, or generalized tuberculosis of the peritoneum, involving the stomach wall; a mass of tuberculous lymph glands, as in Litten's and Hamilton's cases, or an extensive adhesion to a neighboring organ, as in Ruge's, Fisher DeFoy's, Curschmann's and many others, but probably most suggestively illustrated in the case here reported. Surely we must definitely rule out any such cause as this before we grope about among the more obscure possibilities of primary infection through the mucosa.

Classification.

It seems from the foregoing that it is necessary to distinguish several general modes of infection.

I. Those arising from a continuity or contiguity of structure. This is possibly best illustrated by the case here reported. We include in this class cases where there is a tuberculous peritonitis, since the serosa is certainly first affected. This must be the mode of infection, in a vast majority of cases.

II. Hæmatogenous infection as part of a general miliary tuberculosis. This is illustrated by cases of Wilms, Kaufmann, and Simmonds.

III. Those arising from ingestion of tubercle bacilli.

(a) Through a healthy mucosa (that this may occur seems doubtful).

(b) Where there was some factor which predisposed to the infection.

1. Lack of motility and dilatation.
2. Change in the gastric secretion.
3. Slight damage to mucosa as small losses of substance, due to ecchymosis, etc.
4. An increase in lymphoid follicles, as in "gastritis granulosa."

Tuberculous Cavities of the Liver.

Barrier, Rilliet and Barthez first described the so-called gall cysts in the liver of tuberculous children; the latter recognizing their tuberculous origin. Cruveilhier, Foster and others have since described them as simple cysts.

Tuberculosis of the liver occurs most commonly in children, but is not infrequent at any age. Simmonds found 86 cases in 160 dying of pulmonary tuberculosis. While there is some general difference of opinion as to the frequency of occurrence, it seems that the liver is found involved more commonly in acute than in chronic cases, because of the tendency of the lesion to heal (Zedden). Baumgarten in a large series of experimental inoculations, found the liver less frequently affected than the lung, kidney and spleen; no matter how old the experiments were, he rarely found nodules larger than the head of a pin, though these may be very numerous. Cases are reported where a caseous mass, the size of a hazel nut occurred, without cavity formation.

There is no universal agreement as to the occurrence of cavities in the liver. Though they may not be infrequent, their size varies markedly. We often find tubercles with a minute green center. Microscopically these are seen to be small cavities containing duct epithelium, and bile salts. On the other hand we rarely encounter a cavity the size of a hazel nut, and as the size of the cavity increases so the frequency of its occurrence decreases. In four recent autopsies, on cases of generalized miliary tuberculosis, I have found in three, minute cavities, while in the fourth there was a cavity $\frac{1}{2}$ cm. in diameter. Often multiple sections must be made before the tubercle with its green pin-head size center is found, but it seems that they will be found directly in proportion to the care with which one looks for them.

The many conceptions concerning the formation of these cavities, may be briefly summarized in two ideas long ago brought forward. Rokitarsky thought they were the result of softening of a conglomerate tubercle, while Virchow believed them widened bile-ducts, which had undergone caseous degeneration. Jacobson has suggested that Rokitansky's theory of hæmatogenous infection, be divided into two subdivisions; (1) portal, and (2) arterial. Klebs thinks that though the infection might be venous in origin, its spread is effected by the lymphatic channels possible by phagocytic cells which after ingesting the organisms degenerate. The real discussion has hinged about the first two theories.

Barthez and Rilliet, in 1894, thought the infection to be primarily one of the bile-ducts. With them Simmonds, Gilbert, Claude, Sergent, etc. have supported the ascending theory, while Birch-Hirschfeld, Fletcher, Kotlar, Zedden and others have supported Rokitansky. Microscopically the evidence is not convincing for either side. Kotlar describes three cases in which there were multiple cavities. Most of these

contained bile, though a few were free of any trace of bile. These latter likewise contained no duct epithelium and were simply an accumulation of tubercles which had softened in the center. In all of the bile-stained cavities duct epithelium was found. In many cases Kotlar was able to trace this epithelium by serial sections, to some bile passage which communicated with the cavity; in no case could it be said that the epithelium was all of one duct, but rather of many small ones which had gradually been involved in the process. He concluded that the infection must be hæmatogenous, affecting the ducts from without-in and the bile-duct epithelium being more resistant to the process of coagulative necrosis, persists longer, and was therefore seen in the cavity.

Fletcher describes a case with many tubercles in the liver, most abundant in the portal areas. Many of these were quite large, surrounded by a fibrous capsule, in many the remains of a bile duct was seen; while in others softening had occurred, and the duct was destroyed. He concluded that the ducts were secondarily invaded from without, and that the infection was brought in by the portal vein.

Simmonds could trace a large cavity into a single bile-duct. He thought the process started in the periduct connective tissue, and spread into the duct, but that the infection was ascending in origin and that the organisms passed through the epithelium.

Sabourin likewise illustrated a direct communication between a large bile-duct and a cavity.

I have been able to trace several small cavities into a single bile-duct. It seems, however, that such findings are only of value when positive for in the further caseation and degeneration of a small cavity, it is quite natural that many more ducts will become involved from without and that the size of the cavity will rapidly become disproportionate to the size of the duct from which it originally started. That even though its epithelium may resist somewhat longer, it must ultimately succumb to the process with the result that a cavity arising from a single duct will no longer have its original epithelium but have a caseous wall in which many bile-ducts empty. As soon as a duct is invaded the outpouring of tuberculous material will cause inflammatory changes, at least, if not true tuberculous change in the communicating ducts. No matter how the process started, as soon as, even a minute cavity is formed, the ducts must necessarily be important disseminators of the process. It seems justifiable therefore to conclude that the microscope is of little or no value in deciding whether a cavity arose in a duct.

The experimental results are more satisfactory. Gilbert and Claude injected tublercle bacilli into the common bile-duct of animals. After two days, they found marked angiocholitis, tubercle bacilli and round cells surrounding the ducts. They could not find any organisms in the epithelial cells. (Zedden argues that it is difficult to understand how a non-motile organism could pass through the epithelium.) The changes progressed slowly and only after three months did they find tubercles. These were scattered through the entire liver tissue, but in much greater abundance in the portal areas. Some of these latter appeared to be softening. They also injected organisms into the hepatic artery but in no case did they find the initial predominating lesion of the ducts above described, and they think we must take note of this in our decision as to whether the infection is ascending. The objection cited in the above paragraph arises here also. In order to determine the primary changes in the ducts, we would have to examine the tissue before cavities had formed, since there is a continuous discharge of tuberculous material into the ducts as soon as a cavity is formed.

Sergent was able to find the organisms in the bile cavities in every case. He says the reason why they are not usually found, is explained by the work of Brissaud and Toupet. They allowed sputum rich in tubercle bacilli, to remain in bile for some hours and then were no longer able to find the bacilli. This is due to an envelope of bile which forms about the organisms and must be removed before they can be stained. He used the method of Lustgarten: treat organisms with equal parts of alcohol and ether and decolorize with potassium permanganate and sulphuric acid. He also found bacilli in the duct epithelium after injecting them in the common bile-duct. After a large series of inoculations, he concludes that there are two types of infection: (1) Non-systematized, affecting the gall-ducts from without-in, as a result of inoculating animals by the portal vein. (2) Systematized, affecting the bile-ducts from within-out, when the organisms are injected into the common bile-duct.

One of the most important points to decide is whether the bile has any deleterious action on the tubercle bacilli. Zedden examined the bile in 20 cases and only found the bacilli in one. Sergent after inoculating the common bile-duct of a dog with tubercle bacilli, removed the bile from the bladder 78 days later and injected it into a guinea pig which died in 40 days with typical lesions. Kockel has shown that on injecting the mesenteric vein of guinea pigs with tubercle bacilli, many were found in the liver, after the first few days. These rapidly disappeared, some engulfed by phagocytes, some after 18 days showing a form of granular degeneration. Maffini and Sirleo likewise found the organisms undergoing granular degeneration after being engulfed by the liver cells. This suggests the possibility that even though bile may be a favorable medium for their development, the liver cells themselves rapidly destroy the organism.

That some such destruction of organisms must take place in the liver, seems perfectly evident. When we consider the great numbers of organisms which are constantly filtered through its capillaries in a general infection and which certainly must lodge there just as pigments, powdered cinnabar, for instance, and compare this with the rare occurrence of any extensive tuberculous disease, or in fact any infectious process, there remains a great disparity which can only be explained by the death of the organisms in the liver. On the other hand, parasitic diseases of the liver are more common; although amœbic dysentery is much rarer than the ordinary bacillary forms, abscesses of the liver are by far more frequent in the former disease.

Dürck and Oberndorf suggest several possible reasons for the relative immunity of the liver to tuberculosis. (1) Anti-bacterial action of the bile. (2) Phagocytosis. (3) Alexin theory, that the tissue juices of the liver have a specific anti-bacterial action. Starker tried media made of liver tissue, but could find no difference in the growth of tubercle bacilli on it, and on ordinary media. His method, however, was so crude that if there was any anti-bacterial action of the liver originally, it would have been destroyed.

The case here reported is of particular interest in this respect, for on the one hand we have the stomach and liver the seat of marked tuberculous change while on the other hand such organs as the lungs and intestines are practically unaffected. It is well known that experimental inoculations of tubercle bacilli, no matter where they are introduced, most often multiply in the lungs, spleen and kidneys, and cause extensive change; that tuberculosis of the pancreas is a very rare occurrence; that tubercles in the liver are almost always minute and tend to heal rapidly and possibly most striking of all a normal testicle is often found side by side with a caseous epididymis. These are only a few of the pathological anatomical facts which seem to point toward a possible answer to the tuberculosis problem.

The question is not why we have tuberculous cavities in the liver, but why we do not have them in every general tuberculous infection, why the pancreas is never affected and why the testicle escapes, etc. There is only one possible answer. The organisms certainly reach these tissues, but they are unable to develop in them. There must be therefore, some property in common to them, which directly or indirectly destroys the baccillus. If Starker found that tubercle bacilli grew as well in media of liver tissue as on ordinary media, it is probable that his liver media was at fault, or that he destroyed the property he was looking for. A more satisfactory way would be to remove aseptically tissue from various animals and try the growth of the organisms on them without further sterilization.

SUMMARY.

Tuberculosis of the stomach may arise in the following ways:

I. By continuity or contiguity of structure. This is probably the most frequent mode of entrance.

II. Hæmatogenous infection as part of a general miliary tuberculosis.

III. By ingestion of tubercle bacilli.

(a) Through a healthy mucosa.

(b) Where there is some predisposing change in the mucosa.

Tuberculous cavities in the liver will be found directly in proportion to the care with which one looks for them. They are of two general types.

I. Entirely independent of the bile passages and containing neither bile nor bile-duct epithelium.

II. Those containing bile and bile-duct epithelium.

(a) Those arising from an ascending infection of the bile passages.

(b) Those arising from secondary involvement of a bile-duct in a caseous mass.

It is impossible to distinguish these two types microscopically for as soon as a cavity is formed, the bile-ducts will be a factor in the spread of the lesion. It will also be impossible to say whether a cavity has formed from a single bile-duct, for the epithelium will disappear after the cavity has attained any considerable size and its branches will empty into the cavity.

Bile has no deleterious effect upon tubercle bacilli. Tubercle bacilli rapidly undergo degeneration in the liver. This may be due to some natural immunity which the liver shares with other organs rarely affected by tuberculosis as the pancreas, thyroid, testicle, etc.

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A CASE OF SIGMOID KIDNEY.

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(*From the Pathological Laboratory.*)

This case is of particular interest because of the unique shape of the kidney. Morris pictures a case described by Coupland of the same general type of fusion, but where the right kidney, which is the lower, is much smaller than the left; and where the shape of the mass is rather oval than sigmoid. Broesike described a fused kidney very similar to the one found in this case. He was the first one to suggest the name "ren sigmoideum" or "sigmoid kidney" for this type, on account of its resemblance to the Roman letter "S." His kidney, however, does not conform nearly so well to the letter "S" as the one here reported:

N. J., age five months, autopsy No. 2952.

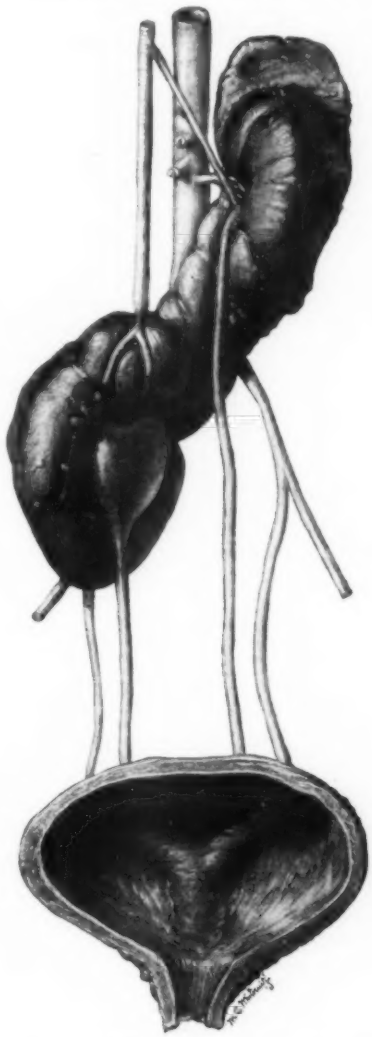
Anatomical Diagnosis.—Acute and chronic ulcerative enteritis and colitis; hyperplasia of the lymphoid follicles of the intestine; emaciation; sigmoid kidney.

After the removal of the intestines, a mass was found lying on the spinal column at the level of the fourth and fifth lumbar vertebra, covering and extending below the bifurcation of the aorta. On examination this was seen to lie sub-peritoneally and to be continuous with the left kidney. The right lumbar fossa, where the right kidney should have been, was hollow and, contrary to what might have been expected, contained no fat. The left kidney seemed to be in its normal position, the upper pole reaching to the level of the eleventh rib. The aorta, vena cava, and retroperitoneal tissue were divided at the diaphragm and carefully removed with the kidneys and pelvic organs.

The two kidneys were then found to have fused, and formed a large "S"-shaped mass, measuring about 8½ cm. in length. It was composed of two distinctly kidney-shaped poles; the upper measuring 4 x 2 x 2 cm. the lower 4½ x 2½ x 2 cm. These were connected by a flattened cylindrical mass of renal tissue, 2 x 2 x ½ cm. in dimensions. Each pole had a definite hilum, the superior facing the mid-line; the inferior, while nearer the mid-line, was directed anteriorly. The ureter of the superior pole, as it entered the hilum, appeared normal; while the calyx of the uterer of the lower mass was bulged out and dilated into a heart-shaped structure, about 1 cm. in diameter. Both ureters entered the bladder in the normal position. The blood-supply, as might have been expected, was anomalous. There were two renal arteries and two veins. The superior artery arose from the aorta at the usual level, and passed directly across to the upper hilum. About 1 cm. before entering the kidney, it divided into two branches: an upper one going to the left adrenal, and a lower larger one which immediately divided again, its upper branch winding around the vein to enter the hilum in front of it, while the lower branch entered behind the lower branch of the vein. Therefore, at the upper position the order from front to back was ureter, artery, vein; while below it was vein, artery, ureter. The two branches of the vein joined a third from the adrenal and emptied into the vena cava (this was collapsed, due to manipulation of removal) somewhat higher than usual. The second artery arose from the ventral side of the aorta about ½ cm. above its bifurcation, and passing in a groove between the connecting cylindrical portion and the lower mass, divided into many branches which entered the renal substance. The last of these wound around to the mid-line and entered the hilum just posterior to the ureter. The two veins, arising anterior to the ureter, soon joined the vena cava. Here the order from front to back was vein, ureter, artery. (There was a small opening on the posterior surface of the cylindrical mass, but what this was could not be determined.)

The left adrenal was in its normal position, but the right, though carefully searched for, could not be found.

McMurrich, in a report of a case of crossed dystopia of the kidney with fusion, collects the cases up to that time, 28 in all. In 15 of these the fused mass was to the right of the vertebral column. In two the mass was crescentic, with the lower pole lying in front of the spine. Usually the hila are both anterior; occasionally, however, one hilum may be in its normal position, while the other, usually that of the crossed kidney, is on the anterior surface.



According to Pohlman the anomalous form of the kidneys may be explained as follows: as a result of some unknown cause, the right renal bud has developed more slowly than the left. He thinks this might be due either to a slower growth of the right bud or to a later date of its appearance, and describes such a retardation of development in embryo, Mall 114 (10 mm. long). As a consequence, in the case reported, the left kidney had reached its normal position and almost entirely rotated, while the right was somewhat lower and had not rotated. In this position the two renal buds had come in contact and fused, the upper pole of the right uniting with the lower pole of the left. As a consequence further rotation or ascent became impossible. We must also consider the possibility that the position of the right kidney might be due to its premature vascularization and consequent anchoring. It has been shown by Hill that the vascularization is entirely dependent on the position of the kidney. Thus a bud which has been slow of ascent might receive its artery from a lower point on the aorta than normal, and by this means be held in a lower position. The occurrence of cases of misplaced kidneys without fusion (Howden, Farquhorsen, etc.) seems to strengthen this possibility.

In the majority of cases of fusion or misplacement of the kidney thus far reported, the adrenal has occupied its normal position. In some cases it has been somewhat misshapen and in others misplaced. Bunner reported only five instances of absence of the adrenal in 48 cases of solitary kidney. In McMurrich's 28 cases, where there is a note concerning the adrenal, it was present in all but one.

Anomalies of the genital tract are much more common accompanying these conditions, but in this case the reproductive organs were quite normal.

In closing, I wish to thank Mr. M. Broedel for his kind assistance and direction in making the accompanying drawing.

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THE RELATION OF BRONCHIAL STENOSIS TO BRONCHIECTASIS.

By W. L. Thornton and J. P. Pratt.

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Inflammatory changes in the bronchial walls and stenosis of the bronchi are generally considered the chief etiological factors of bronchiectasis. At the suggestion of Dr. MacCallum an effort was made to determine the changes resulting from a bronchial stenosis.

In order that the changes of the lungs during respiration might be observed an artificial thorax was constructed (Fig. 1). This artificial thorax consisted of a glass cylinder one end of which was covered by a rubber diaphragm, the other being provided with a tightly fitting glass cover. A rubber stopper with four holes was fitted into the cover. The lungs and trachea, removed from a dog, were suspended within the cylinder by fastening the trachea to a tube passing through one of the holes in the rubber stopper. This tube also served to put the trachea in communication with the outside atmosphere. A canula was inserted into each bronchus, the canulæ being connected to tambours by tubes passing through the rubber stopper. The fourth hole of the stopper was filled with a tube provided with a clamp. By means of this tube a negative pressure could be established in the artificial thorax.

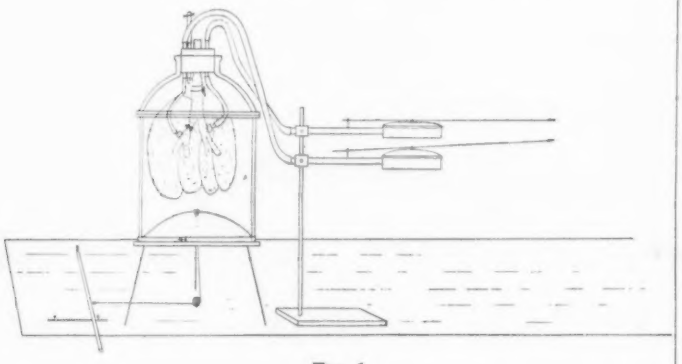


Fig. 1.

Having the apparatus arranged as described above, respiratory movements were simulated by successively pulling down on the rubber diaphragm and then allowing it to return to its original position. The movements of the diaphragm were made by means of a cord which was attached to the center of the diaphragm and passed over a pulley to a lever. The extent of the movements was controlled by moving the lever along a graduated scale.

The bronchial stenosis was produced either by a screw clamp around the bronchus or by placing short pieces of tubes with different-sized lumens inside of the bronchus. Simultaneous records were obtained from the two bronchi, the writing levers of the tambours being superimposed.

When there was no occlusion of either bronchus, the record given by the tambours showed only a slight negative pressure with inspiration and a slight positive pressure with expiration. But when one bronchus was partially occluded the pressure changes in the lung behind the occlusion were more marked; the greater the occlusion the greater the negative

FIG. 2.

FIG. 4.

pressure on inspiration and the greater the positive pressure on expiration. In addition inspiration and expiration are so protracted that the opportunity for a pause no longer exists and they occupy the whole cycle. When the lumen of a bronchus was reduced, the lung corresponding to the bronchus involved, during expiration failed to contract as completely as the lung with an unobstructed bronchus. Owing to this failure to completely contract, an excess of air remained in the lung and the lung remained continually distended, as is shown by the record taken by the tambours (Fig. 2).

The continued distension of the lung may be explained by reference to the diagram in Fig. 3. *a* represents the position of the lung at rest, *b, c, d, e,* and *f* different positions of the lung during inspiration and expiration. When there is no occlusion of the bronchus there will be only a very slight resistance to the ingress or the egress of air. At the end of inspiration the lung will come to the position *f*, then during the expiratory period the elastic recoil of the lung will bring it back to the position *a*. It is evident that the

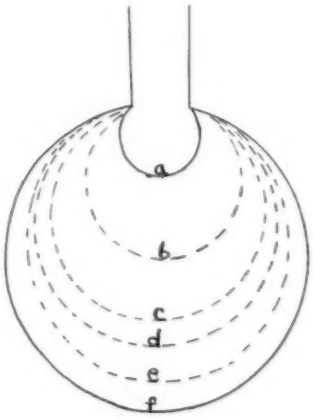


Fig. 3.

force of the elastic recoil will be greater at *f* than at *e*, greater at *e* than at *d*, greater at *d* than at *c; i. e.*, the more the lung is distended the greater will be the force of the elastic recoil, and the more the lung is collapsed the less will be this force. Now if the bronchus be partially occluded the resistance to the passage of air will be increased, and during the first inspiration the lung will be distended only to *c*. The elastic recoil at *c* is not sufficient to bring the lung back to *a* before the next inspiration begins, so the second inspiration begins with the lung at *b* and distends it to *d*. During the following expiratory period the lung recoils to *c*, and so on till a balance is reached between the forces of expiration and inspiration, so that with each inspiration the lung will distend to some point *e* and with expiration will return to some point *d*. Thus it will be seen that the lung continually approximates the inspiratory position.

The relative positions of *d* and *e* will vary with (1) the resistance to the passage of air, *i. e.*, the amount of the occlusion of the bronchus, (2) the time of inspiration and expiration, (3) the elasticity of the lung.

(1) As the bronchus is narrowed *d* will approach *e* till finally, when the occlusion is complete, *d* and *e* will nearly coincide. As the occlusion is removed *d* and *e* will recede till *d* reaches *a* and *e* reaches *f*.

(2) If the inspiratory time be increased *d* and *e* will both approach *f*. If the inspiratory time be decreased *d* and *e* will approach *a*. If the expiratory time be increased *d* and *e* will recede and both will approach *a*. If the expiratory time be decreased *d* will approach *e* and both will approach *f*. If both inspiratory and expiratory time be increased *d* and *e* will recede from one another. If both be decreased *d* and *e* will approach each other.

(3) Although no attempts were made to alter the elasticity of the lungs, it is evident, since expiration depends upon the elastic recoil of the lung, that any interference with the elasticity of the lung would alter expiration; and it would seem that if the walls were weakened the distension would be very much greater than in a normal lung.

In Fig. 2 the upper curve was taken from a tambour connected with an unoccluded bronchus, and the lower curve from a tambour connected with a bronchus that was partially occluded. In the upper curve the expiratory pressure balances the inspiratory pressure with the first respiration and when the respiratory movements stop the curve comes at once to zero or atmospheric pressure. In the lower curve the negative pressure of the first inspiration is as great as or greater than any of the succeeding inspirations, but the positive pressure of the first expiration is small and it gradually increases with the succeeding respirations till it balances the negative pressure of inspiration. When the respiratory movements cease the curve does not immediately come to zero, but falls gradually, showing that air has been entrapped and slowly leaks out.

What has been represented here as taking place in a few respirations must appear very gradually as a result of bronchial stenosis due to the pressure of a tumor or swollen gland, or some similar cause. If a foreign body lodged in a bronchus the above changes might follow very rapidly.

Much stress has been laid upon the increase in intrapulmonic pressure produced by coughing and by such occupations as glass-blowing and playing of wind instruments, in all of which there is a forced effort at expiration against a closed glottis or against an obstruction. A manometer connected with a bronchus would show a great rise in pressure during coughing, just as the manometer connected with an occluded bronchus shows in the model a great elevation of pressure when coughing is imitated. In Fig. 4 such an experiment is carried out with the instrument described above and the upper curve *C* shows the pressure in the occluded bronchus while *B* is the line of atmospheric pressure. In the lower curve, which represents intrapleural pressure, *D* is the line of atmospheric pressure, *E* the line of lowered pressure when the air is sucked out to produce the conditions under which the curve is traced, *F* is the curve made by the same imitations of cough as in the upper tracing. Above, *A* is drawn at a distance from *B* which exactly represents the negative pressure which exists

in the pleural cavity. Now a sudden pressure on the elastic diaphragm of the model with simultaneous occlusion of the bronchus or trachea will represent a cough, and several instances are shown in the curve. It is seen that the pressure in both bronchus and pleura rises greatly and that in form the curves are identical. Curve *F*, however, starts from a negative pressure which really represents the tension necessary to overcome the elasticity of the lung and maintain it at the degree of distension existing during the experiment. Curve *C* starts from atmospheric pressure. The excursion due to cough measures the same and therefore the pressure in one of these attacks of cough is greater within the bronchus than within the pleura by the elastic recoil of the lung. Of course, the relation between the pressure due to the elastic recoil and that due to increased thoracic pressure is very much exaggerated in experiments with this small apparatus.

From these considerations it is evident that in any such act the pressure within the bronchi is greater than that without only by the effect of the elastic contraction of the lung. Otherwise all that portion of the bronchus which is within the pleural cavity and exposed thus to the pressure of the thorax is supported on all sides by the lung tissue, which is subject to the same pressure, and there can be no tendency for it to dilate. On the contrary those parts of the bronchus and the trachea which are outside the support of these compressed tissues are exposed to a distending internal pressure which may be rather high. It is true, however, that during cough the tension under which the air exists in the lung and bronchi is greatly increased, and the same thing occurs in glass-blowing and the playing of wind instruments. This probably could result in a squeezing out of the blood that to some degree might interfere with the nutrition of the pulmonary tissues and may play possibly a part in the genesis of emphysema or even bronchiectasis. This is true in cough only during the actual preparation for the explosive outburst of air from the lungs, and in glass-blowing, etc., only during the actual effort at blowing which follows the deep inspiration. It is therefore of so intermittent a character that its effect in producing malnutrition of the tissue seems doubtful. In the case of a partial obstruction of the bronchus, on the other hand, where the hypertension in the alveoli as compared with that in the normal alveoli is associated with a constant passive overdistension with an excessive amount of air, the conditions to which the bronchial and alveolar walls are exposed are much more serious and really likely to produce damage. It is on this account that we think that such partial obstruction and consequent passive overdistension is probably a fundamental factor in the production of bronchiectasis and emphysema, and its importance is enormously increased when there is associated with it an inflammatory process which may weaken the bronchial wall.

SUMMARY.

The partial occlusion of a bronchus causes air to be entrapped and the bronchus distended, with greater changes in pressure behind the obstruction during respiration. In coughing and related processes the pressure inside the bronchus is greater than the pressure outside the bronchus only by the force of the elastic recoil of the lung; so there is no marked tendency on the part of the bronchi to undergo dilatation.

ON THE OCCURRENCE OF NEWLY-FORMED LYMPHATIC VESSELS IN MALIGNANT GROWTHS.

WITH A DEMONSTRATION OF THEIR ORIGIN AND INGROWTH IN THE METASTASES OF A ROUND-CELLED SARCOMA.

By H. M. EVANS, M. D.

(*From the Pathological Laboratory of the Johns Hopkins University.*)

A search of the current literature, both in medical journals and that in the more important works on the subject,[1] has not revealed the report of any instance in which proper lymphatic vessels were found growing in malignant tissue. The present case, then, is of peculiar interest in this respect; nor does our knowledge of the genesis and behavior of the lymphatic system in general, in spite of recent researches, forbid as superfluous the record of an instance in which both the origin and ingrowth of these vessels seem especially clear.

Practically as old as the recognition of new growths themselves is the knowledge that they possess a blood supply, often, indeed, especially rich. And, though a matter of some doubt until recently, it would appear that nerves are distributed in such tissues.

Borst,[2] in referring to lymph vessels in tumors, recognizes that almost nothing is known about them and consequently hardly discusses the subject. He mentions however that von Heukelom trys to explain the degeneration of many tumors as due to the lack of these drainage channels—an opinion

[1] Such as Borst, Ribbert, Ziegler, Lubarsch-Ostertag, Thoma, etc.

[2] Borst says that according to Ziegler, though lymph vessels had not been proven to exist in sarcomata, irregular spaces and canals in many such tumors must be considered as lymph channels. Such an instance he gives in his Tafel XV, Fig. 83, Bd. I, "Die Lehre v. d. Geschwülsten," Wiesbaden, 1902. The interpretation, of course, is admittedly questionable.

obviously of little value when unsupported by facts. That lymphatics are lacking in such growths is itself an hypothesis even though their presence has never been proven. Those familiar with the delicacy of these structures and with the impossibility of their certain recognition without special methods of study, among which some sort of artificial injection is of prime importance, will not regard the lack of any reports of their occurrence as significant unless these means of investigation have been employed. For though perhaps no general deduction had better be drawn from a single case, it is not impossible, now, that many sarcomata and carcinomata would be found rich in lymphatics were injections of these vessels in fresh tissue repeatedly attempted.

The important researches of MacCallum, Sabin, and Lewis, among others, have solved the riddle of the origin of the lymphatic system, and have shown its later morphological independence as a distinct system of endothelial-walled vessels, not related either to the serous cavities or to the connective tissue spaces with which it has so long been confused, for the lymphatics grow by budding at the tips of their capillaries.

That the lymphatic system possesses some power of regeneration or rather new growth in the adult body has been shown by the work of Coffin, who, at MacCallum's direction, tested this question by producing granulation tissue on the bowel wall in a dog and afterwards injected the lymphatics of this region to find them clearly leading into the young scar tissue.

The present case relates to a patient, F. B., 30 years of age, admitted to the surgical service of the Johns Hopkins Hospital, Sept. 28, 1907, suffering from a marked swelling of the neck of some fourteen months' duration. He died and came to autopsy Nov. 26, 1907. Neither the detailed clinical history [3] nor the entire autopsy report [4] will be given here, but suffice it to say that the case was clearly one of round-celled sarcoma —in the words of the autopsy protocol, "large round-celled sarcoma probably arising in the cervical lymph glands of the left side with involvement of the cervical, inguinal, mediastinal, mesentric, axillary, epitrochlear lymph glands and the following organs: liver, spleen, kidneys, adrenals, peritoneal surface of bladder and the mucosa of the stomach and intestine."

The patient had but a few hours before the necropsy partaken of his usual morning meal and, on abdominal section,

[3] I am indebted to Professor Halsted for permission to add here a few notes from the clinical history of the case. The patient had first noticed a swelling below his left ear at the angle of the jaw about fourteen months previously. The swelling was entirely painless. Within the last six or seven weeks, this had grown rapidly in size and had formed a collar about the neck. For the last six weeks he stated he had suffered from repeated night sweats, and had lost weight. The examination on admission showed a remarkable collar-like mass, "extending from the parotid and posterior auricular region on one side to the same region on the other side along and under the inferior maxillary bone. The mass, which on palpation is made up of a chain of enlarged but discrete non-adherent glands of varying size, starts at the parotid and posterior auricular region of the left side and from here may be traced downwards along the outer side of the left inferior maxillary bone and then over to the right side under the chin stretching inwards as far as the hyoid, and then upwards, running into a large prominent mass in the posterior auricular and parotid region of the right side. Over the mass there is no redness, tenderness, nor sign of inflammation. The mass is composed of glands varying from pea-size to others four or five centimeters in diameter, all discrete, non-fluctuating bodies. The smaller glands are hard, the larger ones somewhat elastic and softened." There seemed to be a deep attachment under the chin, though the masses were generally freely movable. There was also a tonsilar and general glandular enlargement (epitrochlears, inguinals, femorals, axillary, etc.). Up to the last two weeks of his stay in the hospital, the patient was able to be up and about the ward although complaining of weakness and of some œdema of the legs every evening. Towards November 1, the patient complained somewhat of abdominal pain especially along the costal margin. Examination from time to time revealed the presence of palpable nodular tumors which were quite freely movable and interpreted as enlarged mesenteric glands. For the last two weeks he was unable to get out of bed from weakness and died rather suddenly an hour or so after breakfast on the morning of November 26.

[4] I wish to thank Dr. M. C. Winternitz, who kindly gave me the tissue here described, and from whose report I briefly quote. The nodular metastases in the various viscera mentioned are described: "Large masses of glands were found in the supraclavicular fossæ and extending up along the border of the sternomastoid muscles. These joined a collar which formed about the neck below the lower jaw. . . . . The anterior mediastinal glands were likewise much enlarged. . . . . The root of the mesentery is occupied by one large mass of enlarged lymph glands. These vary in size from small ones, the size of a pea, to large ones measuring about 5½ x 3½ x 4 cm. Intestine.—The mucosa, beginning at the duodenum, is markedly thickened, the villi standing out prominently even in the ileum. These are definitely firm and resistant. In places, they form small tumor masses. These vary in size from ½ to 2 cm. in diameter. The larger ones show a distinct hæmorrhagic center, while still larger ones show marked ulceration, leaving a dirty ragged base. In other places, they stand out as large, button-like masses. The colon shows a few of these small tumors.

"Microscopical Notes.—Lymph glands. Nothing remains of the original structure except a few bands of fibrous tissue running in from the capsule. The gland is transformed into a homogeneous mass of cells, between which bands of connective tissue containing blood-vessels can be made out. These, however, are not arranged in any definite system. The cells composing this tumor mass are large, either round or oval in form, the nuclei composing about three-fourths of the cell. These nuclei stain palely with hæmatoxylin, have a definite nuclear network in which masses of deeply-staining chromatin are scattered irregularly. The nuclear membrane is definitely made out. The cell protoplasm is small in amount, stains faintly with eosin, and is finely granular. All stages of mitosis are seen in these cells. Occasionally a nucleus is seen which stains deeply with hæmatoxylin and shows no structure. Other cells are seen which contain several nuclei. They are of many sizes and in places, they seem to be grouped around blood-vessels in concentric rings. Intestine.—The mucosa of the intestine is converted into a large tumor mass in places. This as a rule is made up of well-preserved cells covered on its surface by a layer of necrotic tissue. This tumor mass here is confined entirely to the mucosa. It does not seem to invade the submucosa at all. The masses are of varying sizes, in some places showing only as large papilla-like folds projecting into the lumen of the bowel. Sections taken from the duodenum show the villi to be thickened particularly on their mucous surfaces."

on both the intestine and its mesentery was seen an exceedingly clear and beautiful picture of chyle-filled lacteals. The case afforded so excellent an opportunity for a lymphatic injection of the normal human intestine, it was thought, that pieces of the upper jejunum were taken for injection and study. These coils were distended with warm water, tied off, and their mesenteric vessels ligated. By careful sub-serous punctures with a No. 28 hypodermic needle, using India ink as the injecting medium, the larger, superficial, and much-distended lacteals were quickly filled, even against their valves —a procedure which in most instances would have been difficult in the case of the human bowel. The injection stream could also be seen at many places sinking by way of the communicating channels into the intermuscular and deeper levels. Dehydration, clearing, and further study of the intestinal wall showed that in several places the large submucosal lymphatics were filled and in addition even those of the subjacent mucosa. The study of the lymphatic injection in this last tunic showed that one of those areas in which the mucosal lacteals were filled contained several of the many sarcomatous nodules which were found here. Closer study immediately disclosed a delicate system of lymphatic vessels in the little tumor masses, one of which was embedded in paraffine and cut into serial sections five microns thick, while another was halved and mounted in damar to be viewed with the binocular microscope. Figure 1 is drawn from the latter specimen, while Figure 2 is from one of the sections.

The delicate lymphatic channels of the sarcoma nodule are easily seen to be in direct connection with the pre-existent and neighboring lymphatic plexus of the mucosa, a simple meshwork of anastomosing lymph capillaries resting on the muscularis mucosæ. The serial sections entirely confirm this fact. The new lymphatics have arisen from the mucosal system of vessels and study of the periphery of the tumor mass shows well the method and various steps in this outgrowth. It should be mentioned that the villi adjoining these nodules are enlarged and bulbous, made so, as the sections prove, by sarcoma cells which have extended there in the course of the peripheral growth of the nodule. In these boundary villi between the normal mucosa and the tumor there were observed to arise short finely-tipped outgrowths of the central villus lacteals. At the very edge of the sarcoma these outgrowths were much longer, but still referable to villus lacteals, while in the center of the nodule the new-formed lymphatic sprouts were in such abundance as to obscure the relatively few original mucosal lacteals from which they took origin.

The serial sections, stained after the usual methods, show everywhere that the injection mass was confined in definite channels lined by endothelial cells. Figure 2 shows the tip of one of these lymphatic sprouts cut in a fortunate plane, whereby one observes the proliferating endothelial cells of the advancing vessel. These appearances correspond in all respects with what has previously been observed in growing lymphatic vessels.

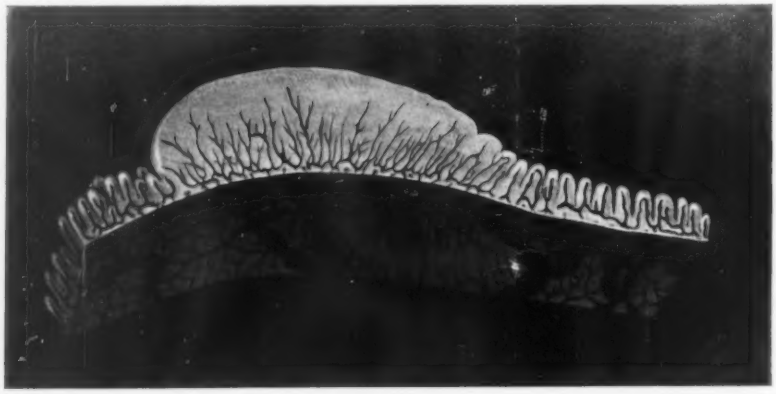


Fig. 1.

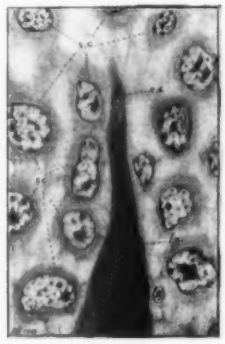


Fig. 2.

It is perhaps important to note that it is the lymphatic capillaries, *i. e.*, merely endothelial-walled vessels without valves and the finest vessels of the lymphatic system here, which have shown this power of growth. And it is entirely probable that in every instance regenerative or proliferative power in the case of the blood- and lymph-vascular systems is manifested primarily by their capillary bed.

The sarcoma nodules in question, then, appear to furnish the first certain instance of a lymphatic vascular supply to malignant tissue, a discovery which might better have been expected, perhaps, in other and larger tumors, but which is especially easy to confirm in lymphatic-rich territories. Whether, in the further growth of these metastases, the lymphatic vessels would have continued their growth, it is impossible to answer with the material at our disposal, but the original stimulus, doubtless chemical, could hardly have been lessened in such a case.

In conclusion, I wish to express my thanks to Professor W. G. MacCallum and to Professor Mall.

A PRELIMINARY REPORT UPON THE EFFECTS OF FEEDING ANIMALS UPON AN IODINE-FREE DIET.[1]

By A. R. DOCHEZ, M. D.

(From the Hunterian Laboratory, Johns Hopkins University.)

The object of the present investigation has been to produce, by experimental methods, some definite change in the histological structure of the thyroid gland in animals. In view of the fact that the thyroids of many dogs, as they are received in the laboratory, exhibit histologically a picture very suggestive of glandular hypertrophy, and resembling that seen in exophthalmic goitre in man, an attempt was at first made to induce this change experimentally.

That such a change could be produced by excising considerable portions of the gland has been known for some time. The object of the present study was not, however, to bring about a compensatory hypertrophy, but to attain the same result by causing slight injury to the thyroid tissue, and in that way possibly to stimulate the cells to increased growth and activity. Small amounts of silver nitrate were used to produce the injury. One lobe of the thyroid was carefully dissected out and a small piece of the gland (too small to cause any compensatory hypertrophy) was excised to be used as a control in noting any change that might take place. The superior thyroid artery was then exposed and a weak solution of silver nitrate injected directly into the blood supply of the gland, through a small branch of the artery. The amount of silver nitrate injected was 1 cc. and the strength of the solution varied from 0.2 to 0.8 per cent. The results obtained, as far as accomplishing the object of the experiments is concerned, were negative in all the dogs treated. About one-half of the animals died of broncho-pneumonia within three weeks after the operations. The thyroids, upon microscopic examination, all showed evidences of injury. Many of the alveolar cells were desquamated and necrotic, and there was a marked increase in the amount of connective tissue varying in amount with the strength of the solution used. Three of the dogs lived four months. The thyroids of two of these animals showed a moderate degree of sclerosis, and that of the third had entirely disappeared, and in its place was found nothing but a ribbon-like band of connective tissue.

When it was found that the above methods did not offer a very hopeful means of solving the problem, Doctor MacCallum suggested that, in view of the apparently important relations of iodine to thyroid activity, it would be interesting to attempt to deprive animals of their natural supply of iodine. On account of the difficulty of contriving an artificial food which should contain the necessary proportions of salts, it was considered best to find, if possible, a natural food which contained either very little or no iodine. A number of food-stuffs were examined, and their iodine content determined by the method of Gautier and Bourcet. The following table shows the results obtained from this analysis:

Food.	Amount.			Iodine Content.
Neuchâtel cheese	100	gm.	(dry wt.)	0.05 mg.
Cow's milk	900	"	"	0.04 "
Cane sugar	105	"	"	0.38 "
Crystallized sugar	60	"	"	0.015 "
Crystallized sugar	65	"	"	0.076 "
C. P. Glucose	50	"	"	0.05 "
C. P. Lactose	50	"	"	0.00 "
Egg albumen	35	"	"	0.00 "
Egg yolk	115	"	"	0.15 "
Chocolate (unsweetened)	60	"	"	0.00 "
Hog brain	58	"	"	Trace.
Hog brain	75	"	"	0.015 "
Hog brain	55	"	"	0.01 "
Almonds	60	"	"	0.00 "
Pig embryos (with thyroids)	75	"	"	0.019 "
Pig embryos (with thyroids)	75	"	"	0.045 "
Thyroids of 4 pig embryos				0.02 "
Thyroids of 4 pig embryos				0.038 "
Pig embryos (thyroids excised)	365	gm.	(wet wt.)	0.00 "
Thyroids of above				0.02 "
Pig embryos (thyroids excised)	530	gm.	(wet wt.)	0.00 "
Thyroids of above				Trace.

An examination of these results shows that with the exception of hog brains and pig embryos, those substances which contain no iodine are unsuitable for feeding animals over a long period of time. In the early experiments white mice were used, but as they did not thrive upon the diet of chocolate and almonds, many of them dying within a few days, dogs were substituted, and the foods used were at first hog brains, and later pig embryos from which the thyroids had been excised. In the earlier part of the work, the diet of the dogs consisted exclusively of hog brains and distilled water. Inasmuch as hog brains contain a small amount of iodine, each dog received from 0.01 to 0.02 mg. of iodine daily. Estimations show that the ordinary diet of a dog in the kennels per day contains 0.23 mg. of iodine, a little more than ten times the amount received upon a diet of brains. Difficulty was experienced in keeping the dogs in good condition on account of the apparently irritating effect of the brain upon the gastro-intestinal tract. Many of the animals vomited soon after feeding, and all of them suffered more or less constantly from diarrhœa. This so lowered their resistance that many died within a few weeks of broncho-pneumonia or distemper.

When it was discovered that pig embryos contain only a minimal amount of iodine and that this small content is apparently entirely localized in the thyroid, the diet was changed from brains to pig embryos from which the thyroids had been excised. Although the animals lost considerable weight upon this diet, still their general condition was very

[1] Aided by a grant from the Rockefeller Institute for Medical Research, New York.

much better and the promise of life longer. Distilled water has been used for drinking purposes throughout the experiments. The animals have been kept in cages continuously, so that no other food than that given could be obtained.

In the following histories four of the dogs were fed on hog brains and three on pig embryos. The period of life has varied from 14 to 64 days. In each case a small piece of thyroid, to be used as a control, was excised at the beginning of the experiment.

Dog 2607. Diet hog brains. Duration of life 32 days. The dog was bright and active at the beginning of the experiment but soon began to lose weight, and during the last two weeks suffered continuously from bloody diarrhœa. The animal lost ⅝ of its original weight. The cause of death was intestinal hæmorrhage and ulceration due to parasitic infection. The thyroids were pale and opaque but otherwise normal. Histological examination of the piece excised showed marked irregularity in the form of the alveoli. The epithelial cells were high cubical in form. The colloid was subnormal in amount. The portions at autopsy showed the alveoli still somewhat irregular in outline. The epithelial cells were high. The colloid was absent from some of the alveoli, but others showed the presence of a good deal. In comparing the two sections it was found that the colloid in the thyroid at autopsy was increased, otherwise there was no change. Weight of the thyroids 0.28 gm. Iodine content 0.38 mg.

Dog 2807. Diet hog brains. Duration of life 14 days. The animal suffered constantly from bloody diarrhœa and became much emaciated. At autopsy the thyroids were quite pale but normal in other respects. In the excised piece the alveoli were lined with low epithelium, were fairly regular in outline and contained colloid. After feeding the alveoli were apparently much larger and contained more colloid, which seemed to penetrate into the intra-alveolar spaces. The lining epithelium was flattened. Wet weight of thyroids 0.55 gm. Iodine content 0.023 mg.

Dog 1708. Diet hog brains. Duration of life 51 days. The dog became progressively thinner throughout the experiment, losing six pounds, one-half of its original weight. During the last three weeks the animal was very weak, being scarcely able to stand. The gums and lips became swollen and spongy, and at autopsy exhibited a gangrenous condition. The cause of death was broncho-pneumonia. Both lobes of the thyroid were of the same size and were somewhat smaller than normal. They were so translucent that the vessels within the depths were easily visible. The consistency was slightly increased. Microscopical examinations of the excised piece showed marked infolding of the alveoli, and high cubical or cylindrical epithelium. There was relatively little colloid, and great variation in the size of the alveoli. The thyroid after feeding presented practically a normal appearance. The whole gland was made up of round alveoli lined with flat epithelium. The alveoli were filled with homogeneous colloid. In this animal there is a reversion from a distinctly hypertrophied thyroid to the normal type of gland with marked increase in the amount of colloid in the alveolar spaces. Wet weight of thyroid 0.55 gm. Iodine content 0.27 mg.

Dog 2108. Diet hog brains. Duration of life 14 days. The animal had diarrhœa from the start and rapidly became much emaciated. The cause of death was broncho-pneumonia. The thyroids at autopsy were quite normal in appearance. The excised pieces showed great variations in the size of the alveoli, only the larger ones containing colloid. They were irregular in outline and lined with high cubical epithelium. The thyroid after feeding was much nearer to normal in appearance. It was composed of alveoli of fairly uniform large size, lined with flat epithelium and distended with colloid. Iodine content 0.18 mg.

Dog 2808. Diet pig embryos. Duration of life 43 days. There was a loss of .five pounds in weight during the experiment. The cause of death was broncho-pneumonia. The thyroids appeared to be somewhat larger than at operation and slightly firmer than normal. The excised piece showed alveoli of moderate size and somewhat irregular outline. But few of the alveoli contained colloid. The epithelium was cylindrical in type and showed some infolding. In the thyroid at autopsy there was a definite increase in the size of the alveoli. Slight irregularity in outline was still apparent. The alveoli were filled with colloid. The epithelium was cubical in type and showed no infolding. Wet weight of gland 1.45 gm. Iodine content 0.29 mg.

Dog 4708. Diet pig embryos. Duration of life 14 days. The animal was quite healthy up to the 14th day of the experiment when it died suddenly. The autopsy revealed extensive broncho-pneumonia. The thyroids showed slightly increased consistency. The excised piece of the thyroid was normal in appearance. The thyroid after feeding showed no very apparent change. There was possibly a slight increase in the average size of the alveoli, and in the total amount of colloid. Wet weight of thyroid 1.0 gm. Iodine content 0.5 mg.

Dog 3308. Diet pig embryos (thyroids excised), 15 gms. C. P. lactose, and 20 gms. lard per day. Duration of life 72 days. The animal became progressively thinner and weaker during the experiment and at the time of death was extremely emaciated. The autopsy revealed no other anatomical lesions as the cause of death than the extreme emaciation and apparent starvation. The hair had fallen out in patches over the forehead, ears and sides of the neck. Over the chest numerous smaller areas were completely devoid of hair. The hair did not grow out over the shaved incision. There was marked œdema of the subcutaneous tissues of the anterior portion of the neck. A less marked degree of œdema extended over the chest and back. The fat in the subcutaneous tissue had disappeared and its place was occupied by an œdematous tissue from which fluid exuded on incision. The organs were all normal with the exception of the liver, which showed focal necroses. Both thyroid lobes were large and very firm. They were extremely pale amber in color, and so translucent that blood-vessels could easily be seen in their depths. The alveoli were enlarged and could be distinguished with the naked eye.

Microscopic examination of the piece excised before the experiment shows a practically normal gland. The alveoli are lined with flat epithelium and contain abundant colloid. In the thyroid, after feeding, the alveoli are uniformly round and quite large. They contain very abundant colloid. The alveolar walls are thin and the epithelium flat. Wet weight of thyroid 2.4 gms. Iodine content 0.9 mg.

Consideration of the above results shows that in every one but one the colloid in the thyroid at the end of feeding was more abundant than that seen in the pieces excised at the beginning of the experiment. Those glands which showed a hypertrophied condition have tended to revert to normal with accumulations of the colloid in the alveoli and a marked flattening of the epithelium. With the increase in the amount of colloid several of the glands showed a rather high iodine content despite the small amount of iodine contained in the food.

It has been suggested by Dr. Halsted's work that mere handling of the gland or excision of a small piece might result in hypertrophy. In view of this supposition, the thyroids of 10 dogs were examined after they had undergone considerable handling at operation and after several small pieces had been excised. In two a low grade of hypertrophy was observed. The thyroids of two showed no change, and in six there were distinct evidences of increased colloid and flattened epithe-

lium. Whether the increase in the colloid content of the thyroids in the experimental animals was due to the diet, or to the diminished call of the tissues for thyroid secretion because of the inactivity of the caged animal, has not yet been determined. Dogs are now being kept caged and fed on normal diet to see if the thyroid undergoes the same change as that observed in animals fed on iodine-free food.

All of the animals fed lost a great amount of weight, so that the food value of pig embryos is being determined in order to make up whatever deficiency there may be in the amounts of proteid, carbohydrate, fat, and salts. The greatest difficulty has been experienced in keeping the animals free from intercurrent infections. The dogs that are being fed now will be muzzled and turned out into the yard every day so that the normal mode of life of the animal may be duplicated as nearly as possible.

CHANGES IN THE PANCREATIC DUCTS, AND THEIR RELATION TO CHRONIC PANCREATITIS.

By M. C. Winternitz, M. D.,

Fellow in Pathology, Johns Hopkins University.

In a recent autopsy performed at Bay View Asylum, the pancreas presented such an unusual combination of pathological changes that at the suggestion of Dr. W. G. MacCallum it is herewith reported.

History of Case.—J. D., white male, age 49, was for many years an inmate of the almshouse. Towards the end of the past summer he was admitted to the medical wards, complaining of swelling of the legs and pain in the abdomen, especially on the left side. He was found to be suffering with "cardiac breakdown," probably due to chronic nephritis. There was decided pain on pressure in the left epigastric region, though no tumor was felt. Gastric analysis showed: total acidity, 16; no free hydrochloric or lactic acid. It was thought he might be suffering from gastric carcinoma. His condition became steadily worse and he died on September 30, 1907.

Anatomical Diagnosis.—Bronchopneumonia; chronic interstitial nephritis; myocarditis; cardiac dilatation, and hypertrophy; pericardial effusion; chronic mitral, and tricuspid endocarditis (mitral and tricuspid insufficiency); chronic passive congestion of abdominal viscera; arteriosclerosis; pulmonary emphysema; chronic gastritis, and enteritis; localized chronic pancreatitis; adenoma arising in pancreatic duct; bilateral hydrocele; hypertrophy of prostate.

Pancreas is of normal size and consistency. The lobulation is distinctly made out, but not excessively prominent. On section it is semi-transparent, of a dull grayish-white color. The islands of Langerhans are seen as opaque yellowish dots. A probe can be passed from the middle of the gland, through the duct of Wirsung into the duodenum with ease. (A portion from posterior third of pancreas, about 3 cm. in length, was preserved for further study.)

Microscopical Note.—In the lower third of the triangular cross-section were several areas of connective tissue infiltrated with round cells. These contained only atrophic islands of Langerhans (Fig. 1). Besides these areas, several large ducts, much larger than those seen anywhere else in the section, were found lying close together. The epithelium was of the high cylindrical type, but instead of being a single layer of cells, they were arranged in curious folds which projected into the lumen, while lying free in the duct were island-like structures with a layer of similar epithelium about them, and a loose cellular connective-tissue core (Fig. 2).

In an effort to correlate this localized pancreatitis with the changes in the ducts, serial sections were made from the original block. These will be described beginning with the most proximal. Each is a complete cross-section of the gland.

In general, the acinar parenchyma is perfectly normal in appearance, as are also the islands of Langerhans. The interacinar connective tissue is increased slightly throughout. The ducts everywhere are surrounded by a considerably thickened fibrous wall, which is poor in nuclei, and stain intensely with eosin. Around the larger ducts more especially, these hyaline-like areas contain numerous small tubular structures, which in places can be seen budding from the main duct. These are all lined by a single layer of cubical epithelium.

With but little gradation there appear several large bizarre-shaped ducts lying close together, whose epithelial lining is arranged in papillary folds, now appearing as a double row of cells lying base to base, now forming a serrated edge, and in places apparently fusing to form tubular structures lying free in the duct, or island-like structures as described above. Here and there the basement membrane appears broken, allowing these folds to project into the surrounding dense connective tissue. Everywhere accompanying the change in the ducts, the acini are extremely atrophic, occurring as clumps of shriveled cells, while the interstitial tissue is markedly proliferated and studded everywhere with many small ducts and an occasional island of Langerhans still quite normal (Fig. 3). There is a considerable infiltration of small round cells, more marked about the larger ducts, and occasionally a plasma cell or eosinophile is seen. The veins are markedly dilated with blood, while the arteries are contracted and have thickened walls. The epithelium lining these atypical ducts, as that also of the smaller tubules, is no longer cubical but extremely high, staining intensely with eosin, and seemingly full of secretion. The nuclei may be flat, round, or oval, usually pale, rarely staining deeply or showing some stage of division (Fig. 4).

As one passes distalward it becomes evident that one duct shows a greater change than the others. It is markedly di-

lated, while its lumen is filled by a large papillomatous, cauliflower-like epithelial formation. The wall is much thickened by many layers of fibrous tissue, everywhere interrupted by larger or smaller tubules, separated from the lumen of the large duct sometimes by only a few strands of tissue. These smaller ducts followed through a number of sections show all the above described changes of their epithelial coat.

Contrary to what might be expected, the connective-tissue overgrowth is not so marked. Each duct is imbedded in a mass of fibrous tissue, but surrounding these are large areas of adipose tissue interrupted by masses of connective tissue containing islands of Langerhans and ducts of varying forms (Figs. 1 and 3). Occasionally islands of Langerhans are seen isolated in the fatty tissue. In other places where the changes in the duct are not so decided there is a marked chronic interacinar pancreatitis. These degenerations follow the ducts systematically, and it is instructive to note that as the ducts become more atypical in one region and less so in another how the changes in the parenchyma shift their position.

The whole picture becomes more intense as the tail is approached. The altered ducts become more and more numerous. Occasionally one will be found cut longitudinally, showing a more complete system of folds and new sprouts, and in one area apparently breaking up into many ducts of varying size (Fig. 5). The last section shows a cumulative picture of the above changes and at least half of the pancreatic tissue has been destroyed.

Localized pancreatic cirrhosis is not a very common occurrence. McClure reports a case, in which a calculus lodged in the posterior portion of the duct of Wirsung in a dog, caused a similar microscopic picture of the parenchyma as above described. He, however, makes no statement as to the condition of the ducts in the atrophic area; though in the gross he says, minute bulgings could be seen in the proliferated connective tissue, and the main duct was greatly distended. A similar case is reported by Whipple, where the ducts are large and dilated beyond the point of obstruction. Likewise Schmidt, and many others have reported cases, but in the majority of these there is an involvement of the entire pancreas distal to some obstruction.

Herxheimer described five cases, in which the pancreas showed areas where the parenchyma was either entirely atrophied, or only small remnants of the acini remained embedded in dense overgrowth of fibrous tissue. The islands of Langerhans still persisted, showing little atrophy. These areas of sclerosis were rendered the more conspicuous by either lying around dilated large ducts or by having small ducts scattered through them. He thinks this change due to some obstruction of the ducts, which he, however, was unable to find. He theorizes on the possibility of some toxic agent causing a primary necrosis of the parenchyma with the consequent new formation of connective tissue, which might so contract around a duct at some point as to effectually narrow its lumen. This would cause the normal secretion to be dammed back with the above described results. Dieckhoff had previously suggested this. Herxheimer further thinks such a stagnation would favor the formation of calculi, which would assist the process.

There are few pathological conditions of the epithelial lining of the ducts reported. Gutmann, in a case of chronic pancreatitis in which the clinical diagnosis of diabetes mellitus was made, describes the change in the ducts as follows: The main duct, embedded in dense fibrous tissue where the pancreatic tissue is markedly atrophic, is surrounded by numerous small ducts of various forms, lined by a single layer of cubical epithelium. These are occasionally seen to connect with the main duct. In the larger ducts one sees round or forked papillæ projecting into the lumen, and occasionally structures lying free in the lumen, composed of a connective-tissue framework lined by a cylindrical layer of epithelium. He argues that there must be an increase in the ducts here, and that one might speak of an adenomatous proliferation. Lazarus and Steinhaus have described similar cases occurring in connection with cirrhosis of the liver.

Reitmann, in a case of chronic pancreatitis, describes areas where many large ducts unite to form curiously shaped cavities. These ducts are nowhere lined by normal epithelium. One often finds several layers of cells which cover a much-folded basement membrane. There are many small ducts formed by budding processes from the larger ones.

Herxheimer, in a case of chronic pancreatitis, says: "In places where the connective tissue is proliferated most markedly, there are large numbers of small ducts which present a picture of adenomatous change. In several places the epithelial lining had so proliferated as to practically occlude the lumen. These duct changes were present in markedly cirrhotic areas where only ducts and islands of Langerhans were to be seen." Ssobolew, Anschütz, Fleiner, and others have also noted this condition.

Gutmann reports a case of adenocarcinoma of the pancreas with metastases to the liver, peritoneal, and pleural cavities in which he describes the much convoluted ducts lined with a single layer of high columnar epithelium. The nuclei stain deeply, are round or oval, and are placed at the base of the cell. The metastatic nodules have the characteristics of a pancreatic tumor.

Hulst adds two cases of primary adenocarcinoma arising in the head of the pancreas, the first with metastasis to liver, the second to the liver and lymph glands. In these cases the pancreas was not much altered in form. Microscopically the parenchyma was either destroyed or extremely atrophic, on account of the overgrowth of connective tissue, which he thinks was caused by the "sialangitis" and "peri-sialangitis," rather than by the tumor. There were many ducts close together, showing papilli-form proliferations, composed of large, cylindrical cells, with large, oval, pale-staining nuclei usually basal, and occasionally showing mitoses. These ducts were occluded by the proliferations, and in places seemed to break through the duct wall, forming secondary tubules of similar character. He thinks these tumors arise in the ducts of the pancreas, and adds that without the occurrence of metastasis, it would be very difficult, after seeing many cases of acute and chronic

pancreatitis, damming back of secretion, tumor, etc., to diagnose any single case as one of malignant adenocarcinoma. He thinks the diagnosis possible, however, without the occurrence of metastasis, because while the increase in the number of ducts is claimed by some to be explained by simple chronic inflammation, the tubular structures being not really ducts, but the remains of the atrophic parenchyma, he finds that the atrophic acini are surrounded, and separated from each other by newly-formed fibrous tissue, and that their lining epithelium always have the characteristics of resting cells, showing a simple atrophic degeneration. On the other hand, the tubules which are of new formation are much larger, have irregular nuclei, of varying size, form, and chromatin content, with increased amount of cellular protoplasm.

He referes to two other cases found by Seehbohm and Ruggi and says they are found sparsely in the literature. Gutmann reports a somewhat similar case where the tumor developed in the body while the head was normal. The ducts showed practically the above described change. He regards his case similarly as a primary adenocarcinoma of the pancreas, but thinks it impossible to state its absolute histogenesis, inclining, however, strongly to the view that the ducts are the primary seat of change. He quotes Orth, Ribbert, Lubarsch, Kaufmann, Dieckhoff, etc., as considering such growths to arise in the ducts.

On examining a large number of sections taken from normal glands, and those presenting various pathological changes, with special reference to the condition of the ducts and connective-tissue proliferation, several very interesting changes were observed.

1. Chronic pancreatitis of all degrees and types occurs in which the ducts are quite normal.

2. It is not uncommon to find a thick wall of connective tissue about the ducts, even the smallest ones, in a relatively normal pancreas, where there is no other increase in fibrous tissue. In this thickened wall many small ducts can be seen budding from the larger ones. These are usually lined by a single layer of low cubical epithelium (Fig. 6). This has been observed by Langerhans and others who think it a process of regeneration.

3. Here we have all the characteristics of group 2, plus a large dilated duct which is quite frequently of an irregular shape. The epithelial lining is somewhat higher than normal, and curiously enough, the small ducts are usually lined by a similar layer of cells instead of the low cubical variety that one would expect to find in a tubule of that size. These cells are quite uniform, but in one case (J. H. H. Autopsy No. 2263) the nuclei show a more variable shape (Fig. 7). In none of these cases was there any marked constriction along the duct.

4. In this group the ducts are not only dilated and lined by high cubical epithelium, but the epithelium projects into the lumen as papillary folds, often cut in such a way that they appear as the island-like structures above described. It is interesting that two of these specimens (J. H. H. Autopsy Nos. 1867 and 2274) were obtained from cases clinically diagnosed diabetes mellitus. A third case (J. H. H. Autopsy No. 2513) shows the same process in several large ducts lying close together.

5. There is often a marked increase in the number of atypical ducts. J. H. H. Autopsy No. 2583 showed a carcinoma of the papilla of Vater which compressed the common bile duct as well as the pancreatic ducts, causing marked cystic dilatation of the latter. A probe could be passed through the ampulla, showing that the occlusion was not complete. The ducts, however, were not only enlarged but distinctly increased in number. In one area several large ducts, surrounded by numerous smaller ones, filled the field of the microscope (Fig. 9). They were all well preserved and showed none of the retrogressive changes, seen everywhere in the surrounding acinar parenchyma. A similar condition was found in (J. H. H. Autopsy No. 1884), a case of secondary sarcoma of the pancreas, in which there is no marked dilatation of the ducts, but an increase in their number. This increase in the number of ducts found in any single area is probably often to be explained by their concentration following the atrophy of the intervening tissue and by the formation of new sprouts from the old duct in an attempt at regeneration. But as in the case above described, where the ducts were clumped in only one portion of a cirrhotic gland and were all larger than the majority of those found elsewhere, it seems justifiable to conclude that there was a new formation of ducts.

6. The case reported at the beginning of this article and the following one illustrate another group. Here there are numerous large ducts lying close together, showing the peculiar cauliflower proliferations described in Group IV to a far greater extent. At autopsy the duct of Wirsung was considerably dilated. The bile and pancreatic ducts opened separately into the ampulla. Microscopically there was a much dilated central duct, surrounded by large ducts which seemed to arise from it, and which in their turn divided. These were all lined by a high cylindrical epithelium, arranged in folds which only occupied part of the much dilated lumina. These folds often formed tubules, which were free in the lumen or separated from it by varying amounts of fibrous tissue.

7. The most marked changes are shown in the following case. There is a marked fibrous pancreatitis, accompanied by great increase in the ducts which show malignant changes of their lining.

Autopsy No. 2914. Dr. Whipple.

***Anatomical Diagnosis.*—Cholelithiasis (stone in cystic duct with ulceration into duodenum); dilatation of hepatic ducts with subacute cholangitis and abscess formation; peri-pancreatic abscess; extreme chronic pancreatitis with cancerous change; stricture of duodenum; dilatation of stomach, subacute gastritis; anæmia; emaciation; hypertrophy of prostate.**

***Pancreas.*—The tail of the pancreas shows no very striking change, but the head of the pancreas contains very dense elastic tissue which grates under the knife. This tissue appears to be a new growth arising from the head of the pancreas. It consists of a pale pearly-white matrix sprinkled over with yellowish pinpoint opacities. It surrounds the mesenteric vessels closely, and seems to invade the lymph glands in the neighborhood which are pigmented, but show some of this gray translucent tissue.**

There is a small abscess cavity about 2 cm. in diameter between the lower portion of the duodenum and the head of the pancreas which is full of thin turbid yellowish fluid. Microscopically the parenchyma is almost entirely replaced by new growth and fibrous tissue. Here and there masses of small round cells are seen, while in other places accumulations of nuclear debris occur. The tumor is represented by large masses of ducts. These show many different forms, small ones clumped together, large dilated ones, etc. The epithelium lining these, where it is most characteristic (Fig. 10), shows many layers of cells which often appear only as masses of nuclei, the cell division no longer being distinct. These nuclei are of all sizes and show great variation in their chromatin content. Numerous nuclear figures are seen. In places the epithelium has proliferated so much that it extends as a papilla into the lumen. In other areas the basement membrane is interrupted and new ducts formed. The acinar tissue where it has not been entirely destroyed is extremely atrophic, the islands of Langerhans still persisting.

It would be difficult in this case to say which was the primary change. It is well known that cholelithiasis or in fact any simple inflammation of bile ducts, is of great etiological moment in causing hepatic as well as pancreatic cirrhosis (Riedel, Oser, Hulst, etc.). This is particularly so in the head of the pancreas, which might be affected by the inflammation about the bile duct, as it passes through the pancreatic tissue. In this case the chronic inflammation which seems of long standing, may have constricted the ducts in the head of the gland, while the cancerous change developed later. It will be remembered in the case above reported by Hulst, gallstones accompanied the adenocarcinoma of the pancreas. He likewise attributed the pancreatic cirrhosis in these cases to inflammation of the ducts, and thought the malignant change to be secondary. It must not be overlooked, on the other hand, that a large tumor of the head of the pancreas may press upon the ducts and cause an overgrowth of connective tissue due to retention of secretion. Just why damming back the secretion causes fibrous overgrowth and atrophy of the parenchyma is not understood. Opie says the interlobular form of chronic pancreatitis is often caused by duct obstruction, and quotes Carnot, who summarizes the various possible factors which may play a part in this process. Retained secretion, he believes, has a toxic action upon the acinar cells. Obstruction to the outflow of fluid from the ducts favors the entrance of bacteria from the duodenum. Carnot suggests, moreover, that reflex nervous stimuli, which normally reached the secreting cells, are no longer capable of exciting normal functional activity, and deprived of this influence the cells atrophy as do muscle fibres after section of their motor nerves.

More obscure than this are the changes in the duct epithelium following obstruction. With increased pressure in the ducts one would naturally expect a flattening of the lining cells. This is found in some large cysts where either no cells or a flat epithelial lining occurs. In some, on the other hand, occasional clumps of high cylindrical cells are found. In the above cited cases we see dilated ducts with hypertrophy of the epithelium which may form papillæ, new ducts, or a more malignant growth. Similarly it is well known that in cysts of the breast, the epithelial lining is very prone to hypertrophy, forming papillæ, which in turn frequently give rise to malignant growth.

Conclusion.

We have seen several types of change in the pancreatic ducts which seem to gradate into each other. All of these were accompanied by varying degrees of chronic pancreatitis.

1. Simple increase of the connective-tissue wall about otherwise normal ducts.

2. Dilated thick-walled ducts with high columnar epithelium.

3. Ducts in which the epithelium has hypertrophied to form papillæ.

4. Absolute numerical increase of the ducts which may be regarded as a regenerative change and in some cases as an adenomatous proliferation.

5. Ducts in which the epithelium has proliferated to such an extent that not only papillæ but new tubules are formed.

6. Ducts whose epithelium has undergone malignant change.

We have then two definite types of adenoma, or benign proliferation of the ducts, the one where there is a simple increase in the number of ducts, the other where the epithelium of these ducts shows the curious hypertrophic changes described. These two types often seem to merge into one another. Likewise it is often difficult to say when the latter has lost its benign characteristics and become malignant.

The question arises what connection these duct changes have with the chronic pancreatitis.

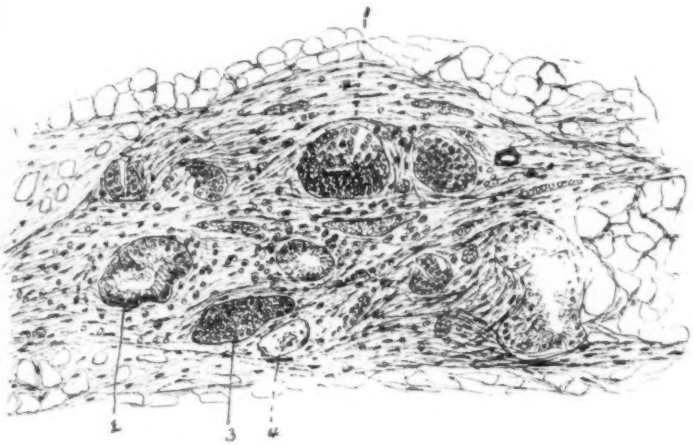
1. The changes in the ducts, particularly their new formation, might be an effort on the part of the pancreas to regenerate after chronic inflammatory processes. This has been suggested by Herxheimer and others, but it seems hardly probable, as the duct epithelium is so entirely different from that of the acini, and shows no gradation anywhere into acinar tissue.

2. This infolding is no doubt sufficient in some cases to cause obstruction to the outflow of secretion and dilatation of the ducts with atrophic changes in the acini.

3. The change in the ducts and the fibrous overgrowth may be due to a third process. In many cases this seems the more likely, as the ducts are much distended, as the result of some form of occlusion, and the papillæ occupy only part of their lumen.

In conclusion, I wish to thank Dr. W. G. MacCallum for his assistance in this work.

N. B.—Since this article was written, another case has come to my notice. Here there was a carcinoma of the bronchus with extensive metastases to the liver. A section from the tail of the pancreas showed several areas of localized pancreatitis. In one of these nothing remained but the islands of Langerhans, and two large ducts whose epithelium was high and infolded. In several other areas the ducts showed hypertrophy of their lining epithelium, and in still others numerous small ducts were grouped about a larger one. Surrounding all of these ducts there was an increase of fibrous tissue, which extended for a variable distance into the neighboring pancreatic tissue.



1. Island of Langerhans.
2. Cross section of duct.
3. Dilated Veins.
4. Artery.

FIG. 1.

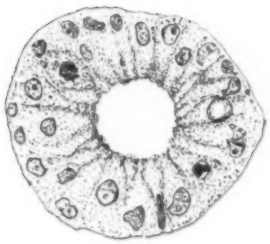


FIG. 4.

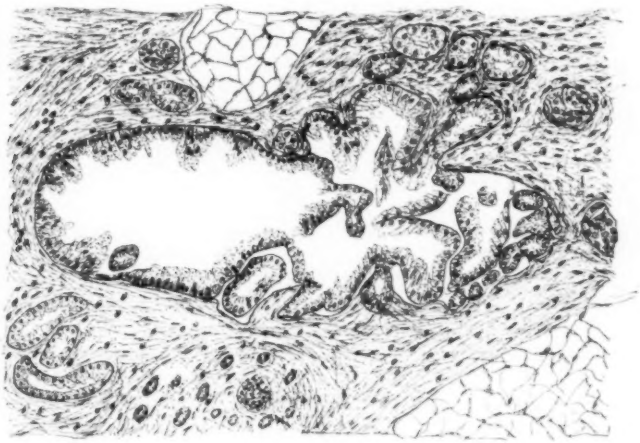


FIG. 2.

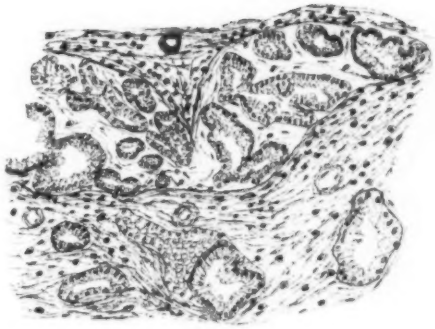


FIG. 5.

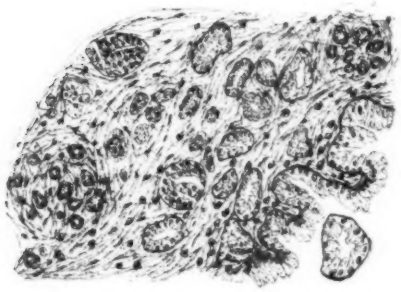


FIG. 3.

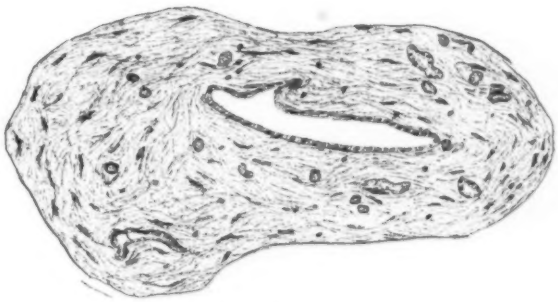


FIG. 6.

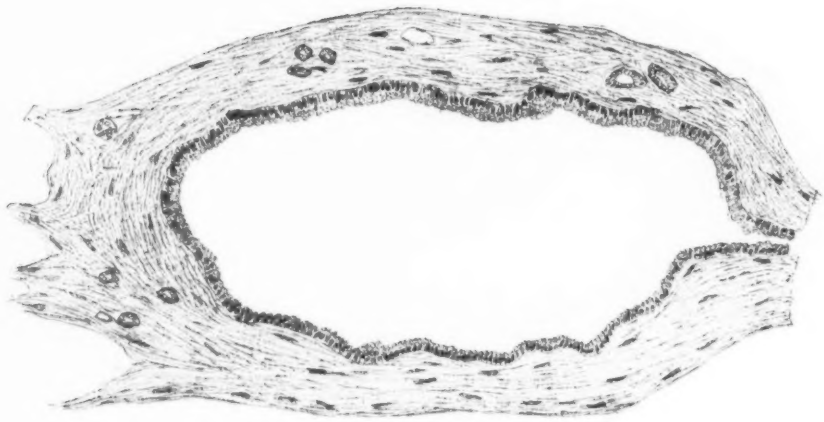


FIG. 7.

FIG. 9.

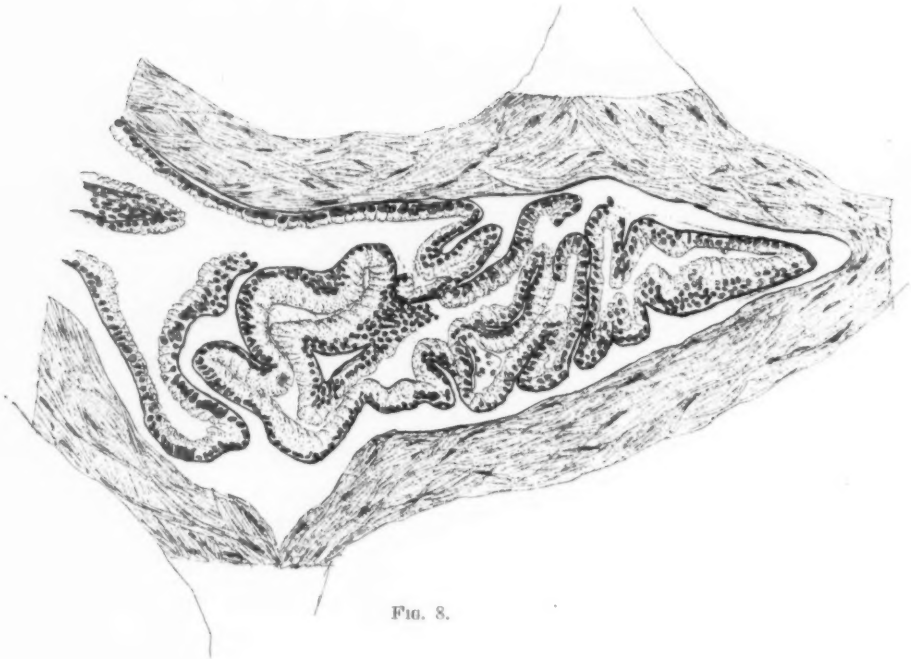


FIG. 8.

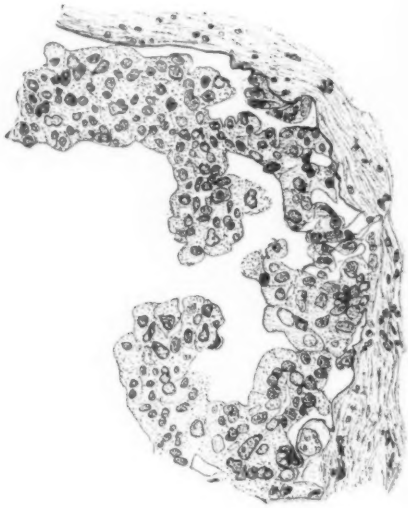


FIG. 10.

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THE PHIPPS PSYCHIATRIC CLINIC IN CONNECTION WITH THE JOHNS HOPKINS HOSPITAL.

Upon the 12th day of June, after several conferences between Mr. Henry Phipps and Doctors Welch, Barker and others, representing the Johns Hopkins Hospital, the following letter was received from Mr. Phipps:

I understand that there is urgent need in this country in connection with university medical schools and their hospitals for institutions similar to those known as psychiatric clinics, to provide for the better care of patients suffering from mental disease, especially in its earlier and often curable stage, under conditions similar to those of a general hospital.

Since patients may enter such an institution without the formality of commitment, and without the stigma which is popularly thought to pertain to admission to an asylum for the insane, experience has demonstrated that many may be rescued from permanent insanity by early treatment in an institution of this character.

A psychiatric clinic, as thus understood, should also afford much needed opportunities for the instruction of medical students and physicians in this important field of medicine, and should be equipped with laboratories for the scientific investigation of the nature, cure and prevention of mental diseases.

It gives me pleasure to offer to the Johns Hopkins Hospital the funds necessary for the erection and equipment of a psychiatric hospital on its grounds, in accordance with the plans and estimates which you have submitted; the institution to provide for about sixty patients, and to contain the necessary laboratories and other facilities, and furthermore to offer to the Johns Hopkins University additional funds for the establishment of a professorship of psychiatry, and the assistantships thereto, the professor to be also the director of the psychiatric hopital.

I have arranged to provide for the maintenance of the hospital and of the professorship for a period of ten years from the time of the opening of the hospital.

It is my desire that in the admission of patients to the hospital preference should be given to applicants from Baltimore, and from those cities with which my life and work have been so closely associated, Pittsburgh, Philadelphia, and New York.

It is my hope and expectation that the psychiatric clinic thus founded may serve as an example of what such institutions should be, and prove to be a stimulus to the establishment of similar hospitals and professorships elsewhere.

This offer was accepted by the Trustees of the Johns Hopkins Hospital at a special meeting upon the 17th of July, in the following terms:

Resolved, That the noble and munificent gift of Henry Phipps, Esq., be herewith gratefully accepted on the terms expressed in the above-mentioned letter, and that the Superintendent be requested to write to the donor to express the sincere thanks of the Board of Trustees for the liberal generosity which he has shown heretofore to the Johns Hopkins Hospital, and for this new expression of his interest in its work; and for the confidence he has manifested in entrusting to the Trustees the task of carrying out his philanthropic efforts to promote the hospital treatment of mental and nervous diseases and thus to alleviate the sufferings of mankind.

Resolved Further, That Henry Phipps, Esq., be requested to allow the new psychiatric clinic to bear his name in perpetuity as one of the departments of the Johns Hopkins Hospital.

Resolved Further, That a copy of these resolutions accompany the letter of the Superintendent to Henry Phipps, Esq.

Subsequently, upon the 19th of June, the Trustees of the University adopted a minute of similar import.

The Trustees of the University and Hospital also united in appointing Dr. Adolph Meyer, Director of the Pathological Institute of the State Hospital of New York, to the position of Director of the Clinic and Professor of Psychiatry in the Johns Hopkins Medical School.

The newly appointed Director of the Clinic is a native of Switzerland and received the degree of Doctor of Medicine from the University of Zürich in 1892, after studies at Paris, Edinburgh, London, Vienna and Zürich. He came to America in 1892 and was made an Honorary Fellow of the University of Chicago for one year and was later Docent from 1893-1895. In 1893 he was also made Pathologist of the Illinois Eastern Hospital at Kankakee and remained in residence there until 1895, when he resigned both positions to accept the post of Pathologist in the Worcester Insane Hospital. He was also Docent in Psychiatry in Clark University. He resigned these positions in 1902, when he was appointed Director of the Pathological Institute of the State of New York and at once entered upon the duties of this position. He reorganized the work of the Institute and brought the different institutions throughout New York into harmonious relations with it. In addition to the routine work of instruction, he made regular visits to institutions to become familiar with the work of their medical officers and held clerical conferences with them. He has always been a voluminous and forceful writer, as the bibliography appended to this note will testify. He was appointed Professor of Psychiatry in the Cornell University in 1904. He received the degree of LL. D. from the

University of Glasgow in 1901. He is also a member of many medical societies.

Dr. Adolph Meyer has accepted the Professorship of Psychiatry and the Directorship of the Clinic and is to begin his service October 1, 1909. He goes abroad at an early day to accompany Mr. Phipps and Mr. Grosvenor Atterbury, the architect selected to draw plans for the building, upon a tour of inspection of the best and newest psychiatric clinics in Europe.

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PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS MEDICAL SOCIETY.

May 4, 1908.

Meeting of the Johns Hopkins Hospital Medical Society, Dr. Hurd presiding in the absence of the president, Dr. Finney.

I. Exhibition of a Case—Ichthyosis Hystrix. DR. LORD.

The case was that of a white child, aged 5 years, who was suffering from ichthyosis hystrix, or congenital warts. The child was born with a brown discoloration of the abdomen, neck, hands, and feet. Shortly after birth warts began to develop throughout these areas of discoloration. During the last eighteen months the warts have increased rapidly. The child has no symptoms except itching. In some places the warts seem to follow the nerve tracts, but in other places this mode of distribution is not so evident. During the past week the patient has undergone treatment with X-rays, but thus far his condition has not improved.

II. The Cause of the "Loco" Disease. DR. CRAWFORD, Washington, D. C.

The speaker described in detail the results of his investigations of the cause of the "loco" disease, a definite, complicated disorder that occurs in range animals and the cause of which has been laid to the eating of certain leguminous plants. In Australia experimental work has shown that the disease occurs in cattle after eating the loco plant.

The symptoms in an ideal or typical case are of two kinds: gastro-intestinal and those referable to disturbances of the central nervous system. Post-mortem examinations have failed to reveal any lesions that may be called characteristic except ulcer of the stomach in some cases and dilatation of the vessels of the dura mater.

Dr. Crawford first fed rabbits an aqueous extract of the plants and found that the animals would die within a very short time with acute symptoms of poisoning. Two hundred grammes of the dried plant would produce the same result. He then fed rabbits with repeated small doses. Such animals emaciated and died usually in 10 days. They all showed peculiar psychical symptoms, which resembled very closely the mental condition of "locoed" range animals. These animals also aborted fairly regularly—another symptom that is common in poisoned range animals. He was able, therefore, to reproduce the important symptoms that occur on the range.

All attempts to isolate an active principle from the plants were unsuccessful until he found barium present in the ash of the dried plants. This metal occurred in very large amount, 200 grammes of the dried plant contained 76 mg. of barium acetate, while another sample of 200 grammes of dried plant contained 173 mg. of barium acetate. He then fed rabbits repeated small doses of barium and found that they developed symptoms of acute and chronic poisoning that were like loco poisoning.

He found that some loco plants have barium in an insoluble form. Such plants, however, are very toxic to rabbits if the animals are given the digested products of the plants. If the barium was removed from such a digested product and an animal was fed on the barium-free residue, the animal was not harmed; but if now the barium was reintroduced, the animal promptly died. There were also some loco plants from particular sections of the country that contained no barium. Every one of these plants was physiologically inactive.

These studies showed that the occurrence of the loco disease depends upon the prevalence of barium in the soil of the ranges over which the cattle grazed, that the metal is taken up by the plants, which upon ingestion produce symptoms of poisoning, and that the barium not only must be present in the plants, but must occur in such form that the gastro-intestinal tract can render it soluble for digestion.

DISCUSSION.

DR. FUTCHER thought it appropriate that Dr. Crawford had brought his work before this society, since it was 7 years ago since Dr. Marshall had reported here the results of a pathological investigation of this disease in Montana. At that time Marshall concluded that the symptoms of the disease were not due to eating the loco plant. He had observed that all the animals suffered from intestinal parasites and he, therefore, considered the symptoms due to this cause. Dr. Crawford

seems to prove conclusively that the disease is due to some inorganic salt, probably a salt of barium.

Dr. Barker expressed his great satisfaction that the loco problem now seemed to be definitely settled. He recalled that 15 years ago brains of cattle affected with this disease were being sent to the laboratory with the view of determining the pathological cause of the affection. For 50 years, at least, investigations have been going on in the effort to solve this problem, and anything throwing light upon it is of the greatest economic importance. He considered this work of Dr. Crawford's as one more instance indicating the tremendous importance of a knowledge of the part played by inorganic substances in the metabolism of animals and plants, a rôle that we are just beginning to understand.

Dr. Hurd recalled that in 1884, while on a ranch in California, he became interested in accounts given by men who had seen "locoed" animals for years. The Spanish word "loco" means crazy, and in the west the term had become almost synonymous with crazy. This gentleman, with whom he spent several weeks on the ranch, gave very graphic descriptions of the condition of the "locoed" animals. The animals seemed to suffer from queer delusions of space, which symptoms were apparently due to disturbances of the nervous system and were fairly constant. On his return from California Dr. Hurd brought with him a large quantity of the plant and submitted it to chemists for analysis, but they did not succeed in making an active extract. It seems that sheep herders when driven by hunger are in the habit of cooking and eating the young pods of the loco plant, but so far as Dr. Hurd knew no case of poisoning had been reported among them. It was, therefore, likely that the poison must be in the plant itself or in mature plants only.

III. Studies on Vencus Blood-Pressure. Dr. Eyster and Dr. Hooker.

This paper will appear in the Johns Hopkins Hospital Bulletin.

May 18, 1908.

Meeting of the Johns Hopkins Hospital Medical Society, Dr. Finney presiding.

I. Hereditary Epistaxis Associated with Multiple Telangiectases of the Skin, Nasal, and Buccal Mucous Membranes. Mr. Hanes.

The speaker exhibited four members of the same family, all of whom were subject to recurring epistaxis and who presented on the face and buccal and nasal mucous membranes small telangiectases. In this same family, in four generations, nine members have been afflicted with the same condition.

Case 1.—Mrs. M. R., aged 53 years, has been subject to severe nosebleed for 43 years. Her mother, who died at 48, was a lifelong sufferer from recurring epistaxis, and had upon her face and lips and within her mouth, numerous red spots, similar to those on the patient's face and lips. The patient's two brothers exhibited practically the same condition. Her own attacks of epistaxis have persisted since childhood and have been extremely frequent. She does not bleed excessively from injuries. With the growth in severity of the epistaxis telangiectatic spots have appeared upon her face, lips, and tongue. During the past two years her condition has grown progressively worse. At present she is very anæmic: her red blood count is 1,500,000 cells, and her hæmoglobin 15 per cent. Her coagulation time is 7 min., 50 sec. Scattered over the face, and especially numerous on the ears and lips, are small telangiectases, ranging from a pin-point to a green pea in size. These also occur in great numbers upon the sides and dorsum of the tongue, the hard palate, and the gums of the lower jaw. They are also present upon the fingers of both hands. Upon the conjunctiva of the right lower lid is a small one.

Cases 2 and 3.—J. F. R., aged 33, and T. R., aged 31, are sons of Mrs. M. R., the first patient. In them the facial telangiectases are larger and more numerous, but the epistaxis is less marked. Though they bleed only occasionally form the nose, they have frequent and profuse hæmorrhages after injury to one of the labial telangiectases. Under the nail of the left middle finger of J. F. R. are two telangiectases which arose after he had accidentally run a large splinter under the nail several years ago.

Case 4.—M. R., aged 18, daughter of Mrs. M. R., has suffered with severe and frequent epistaxis since childhood. This bleeding is usually spontaneous, though it may often result from slight trauma. At present her red blood count is 4,000,000 cells; her hæmoglobin, 78 per cent; and her coagulation time, 7 minutes.

T. R., the third patient, has two children: a son, 8 years of age, who frequently bleeds from the nose and who now has two small telangiectases upon the lower lip; and a daughter, aged 6, who has recurring epistaxis, but who shows no spots on the lips.

The speaker could find only seven such cases reported in the literature, and thought that many such cases have perhaps been diagnosed as hæmophilia. He emphasized, as characteristic features of the disease, its hereditary nature, the severe recurrent epistaxis, and the multiple telangiectases. The disease is serious and had ended fatally in several instances.

II. Relation of Tetany to Calcium Metabolism. Dr. MacCallum and Dr. Voegtlin.

Dr. MacCallum, after outlining a classification of the spontaneous types of tetany, confined his attention to the form of tetany that is definitely the result of parathyroid insufficiency. He described methods that have been used to combat it. Transfusion in dogs will stop tetany, and if a large quantity of inert salt solution be injected after bleeding an animal the tetany stops immediately, only to reappear after a short interval. Feeding of parathyroid emulsions seems to be ineffectual, but injections of parathyroid extract will control tetany.

The tetany seems to be of nervous origin. A muscle, severed from its nervous connections, does not become tetanic. At the same time the removal of cerebral cortex does not seem to affect the distribution of the tetany.

The speaker then gave the results of investigations that he and Dr. Voegtlin have made upon the action of calcium salts upon tetany produced in parathyroidectomized dogs. They found that if into such animals they injected a solution of the lactate or any other soluble salt of calcium (a 5 per cent solution), the dog almost immediately returned to normal. A

definite explanation of this phenomenon is at this time impossible, but the tentative hypothesis was advanced that perhaps the parathyroid glands exercise some control over the calcium metabolism, so that if they are excised or diseased there is an improper assimilation of calcium, which goes through the system without being used.

The speaker referred to Jacques Loeb and J. B. MacCallum, who have pointed out that the precipitation of calcium in tissues brings on twitching. He and Dr. Voegtlin have also found that sodium and potassium salts do not stop tetany in the way calcium does, and that while magnesium salts stop the tetany their toxic action is so extreme that the former action is masked.

The calcium also acts efficaciously if fed by mouth. It has been successfully tried therapeutically on two human beings who have suffered from tetany due to parathyroid insufficiency.

Analyses by other observers of the tissues of infants who have succumbed to the so-called infantile tetany have shown a deficiency of calcium, and the idea is gaining ground that such children may be cured with calcium. The tetany of lactation and pregnancy is perhaps explainable on the hypothesis that there is a calcium deficiency due to the draining of calcium from the system.

Dr. Voegtlin described the chemical results of the investigation. An analysis of the brain, blood, urine, and fæces of tetanic dogs as compared with normal controls revealed the following facts: After parathyroidectomy there takes place a change in the metabolism favoring the excretion of calcium through the kidneys and the intestines. As a result of this the soft tissues and blood are found to contain only half the amount of calcium as compared with normal dogs. One remarkable feature is the change in nitrogen metabolism, which sets in soon after removal of the parathyroid glands. The ammonia ratio is greatly increased, from 5 to 25-40. This points towards the presence in the tissues and circulation of acids, the nature of which has not yet been determined. The ammonia content of the blood is found to be increased. From these data tetany may be explained as a condition in which there is an insufficiency of available calcium, for addition of more calcium removes promptly all of the symptoms.

III. The Results of the Use of Anti-meningitis Serum (Flexner's) in the Johns Hopkins Hospital in 1908. Dr. Sladen.

Before the use of this serum the results of the treatment of the cases of epidemic cerebro-spinal meningitis admitted to the Johns Hopkins Hospital had been as follows: During the years 1889-1907, inclusive, out of a total of 33 cases, there were 21 deaths and 12 recoveries—a mortality of 64 per cent. In all these cases the meningococcus was demonstrable in smears or cultures of the spinal fluid.

During 1908, 19 cases of acute cerebro-spinal fever have been so far admitted. The meningococcus was demonstrable in all of them. Of these 19 cases, all of which received the serum treatment, 16 recovered and 3 died—a mortality of 16 per cent. Of the three cases that died, one was a fulminant case; another was a child, 29 months old, admitted on the fourteenth day of the disease, who died 48 hours after admission from paralysis of respiration after having been kept alive for 16 hours by artificial respiration; and the third was a very stout colored woman who was admitted with a complicating broncho-pneumonia of both lungs and who died 48 hours after the first injection of serum.

Most of the cases are temporarily upset by the lumbar puncture and the injection of the serum. During the injection they usually complain of pain in the knees, or occasionally in the hips, or, as has twice happened, of pain about the rectum with the desire to defecate. These pains persist from 2 to 10 hours after injection, and following the injection there is usually a slight rise of temperature with increased restlessness. Urticaria and erythematous eruptions are not uncommon. It takes from 12 hours to 3 days before favorable signs and symptoms ensue. Favorable cases react to a certain extent after one injection. Some cases require but one injection, while others have taken as many as six. It has been the rule to give the serum daily until the temperature remains normal and to renew injections as soon as a recrudescence occurs.

The first effects are a fall in the temperature (following the initial rise), and subsidence of delirium, headache, pain in the neck and back, and general hyperæsthesia. Strabismus, stiffness of the neck, and Kernig's sign are more persistent, and Kernig's sign is often the last feature to disappear. Pressure signs and symptoms are thus seen to yield readily, although the amount of serum injected may be greater than that of the fluid withdrawn.

In the spinal fluid the polymorphonuclear cells increase in number after the first injection, but gradually disappear during recovery. The meningococcus, mainly extracellular in most cases, becomes intracellular after serum, and shows evidences of dissolution, staining much less distinctly.

IV. Hydrocephalus of Meningococcus Origin. Dr. Knox.

Will be reported later.

NOTES ON NEW BOOKS.

State Board Questions and Answers. By R. Max Goepp, M. D., Professor of Clinical Medicine at the Philadelphia Polyclinic. Price, $4.00. (*Philadelphia and London: W. B. Saunders Company.*)

The author states in his preface that the questions were selected from State Board examination papers, and that the volume "is to provide a convenient compend for the use of those who wish to prepare themselves for such examinations." The questions were not taken from any one State papers, but from those of "the larger and more representative States." The author claims no originality for the answers, many of which are taken verbatim from standard text-books. The contents are arranged under the headings of physics, chemistry, physiology, anatomy, hygiene, materia medica and therapeutics, practice of medicine, surgery, obstetrics,

gynæcology, pathology and bacteriology. The book has an extensive index, so that its use is much facilitated. A little more time given by the author to further classification of the questions would have made the work still more easy of use. It will no doubt, however, be warmly welcomed by a large body of young graduates of the medical schools. R. N.

Hygienic Laboratory, Bulletin No. 40. United States Public Health and Marine Hospital Service, 1908.

Of the four papers in this bulletin by Stiles, and Stiles and Goldberger, the first, in which Stiles described "The Occurrence of a Proliferating Cestode Larva (*Sparganum proliferum*) in Florida" is of special interest to medical men. This remarkable dermal infection has been described but once before by Ijima in a Japanese woman. The infection is characterized by the appearance of pin-point cysts or acne-like nodules in the skin or subcutaneous tissue. These may increase in size to that of a grain of rice. When the cyst is incised or ruptured by pressure, one or more minute plerocercoid-like larval worms may be found in a clear fluid or jelly. These worms have calcareous corpuscles, showing them to be Cestodes, but no genital system or other means of specifically identifying them. They multiply in the cysts by budding, so that as many as 7 worms have been found in one cyst. They vary in size from 0.3 x 3 mm. to 2.5 x 12 mm. and present very bizarre shapes due to the budding. The infection in the skin may reach many thousand cysts, resulting in lymphatic stases and a condition not unlike elephantiasis. The adult form of the parasite is entirely unknown, as is the source of the infection. Both the cases described lived directly on the sea-coast and subsisted largely upon marine fishes and molluscs. It is quite probable that a careful examination of fishermen on our Southern coasts will disclose other cases. Thos. R. Boggs.

Metabolism and Practical Medicine. By Carl von Noorden. Vol. I. Price, $6.00. (*Chicago: W. T. Keener & Co., 1907.*)

The first two volumes of this system have already been discussed in this journal. The volume under consideration is the third and last one and includes chapters on diabetes mellitus, gout and obesity by v. Noorden; rarer derangements of carbohydrate and proteïn metabolism, oxaluria and phosphaturia by Neuberg; cancer by Schmidt; diseases of skin by Salomon and v. Noorden; children's diseases by Czerny and Steinitz; mineral waters and metabolism by v. Noorden and Dapper; bath and metabolism by Matthes; ductless glands by Magnus-Levy; influence of drugs and poisons on metabolism by Loewy; light and metabolism by Salomon; nervous diseases, bone diseases, diabetes insipidus by Mohr.

The last pages are devoted to tables containing the chemical composition and caloric value of practically all the foodstuffs. This is of great assistance to anyone who desires to get information about the composition of a special diet and its value as a food.

Of remarkable interest and well written are the chapters on diabetes, the ductless glands and childrens' diseases. The names of the authors connected with these titles are too well known in the field of original work to leave any doubts of the value of these articles. The facts are brought together in a way that renders reading fascinating.

There is, however, one objection that may be made to this system. It is well known by everyone working in metabolism that there exists in this particular literature an immense amount of what might be termed pseudo-scientific research. Work is done with no regard as to the accuracy of the methods used and conclusions are drawn prematurely.

This system does not sift out enough the reliable data from the doubtful ones, and for this latter reason the beginner in metabolism work will not find the absolute truth of the standing in this field. At the same time we will not omit to emphasize the importance of this book in bringing together practically all the available literature. It is now considerably simpler for a practitioner or anybody else interested in this subject to find a revise of the vast amount of work.

In conclusion we wish only to congratulate the authors for this very admirable system, which can be recommended warmly.

Progressive Medicine. Vol. II. (*Philadelphia and New York: Lea & Febiger, 1908.*)

In this volume hernia is treated by Coley; surgery of the abdomen, exclusive of hernia, by Foote; gynæcology by Clark; diseases of the blood, diathetic and metabolic diseases, diseases of the spleen, thyroid gland and lymphatic system by Stengel; and ophthalmology by Jackson. There is also an index. The reviews of the literature on these subjects are well handled, and the authors succeed in giving a satisfactory résumé of the most recent progress in the history of these diseases. Many of the illustrations are, however, quite worthless, and more attention should be paid to this point by the editors. R. N.

Diseases of the Nose. By Ernest B. Waggett, M. A., M. B. B. C. (Cantab.), Surgeon to the Throat and Ear Department of the Charing Cross Hospital; Surgeon London Throat Hospital, and Throat and Ear Department, Great Northern Hospital. Cloth. 282 pages, with illustrations. Price, $2.00. (*London: Oxford University Press, 1907.*)

In a very condensed way the author gives his views of the present practice of diseases of the nose and throat. This work has much to recommend it to one who desires in short compass the present status of nasal diseases. In his preface the author points out that the book is written to aid general practitioners in their daily work. He emphasizes the value of a proper appreciation of these diseases in clearing up certain obscure cases. Thus "he may cure the subject of chronic bronchitis of twenty years' standing, by draining an antrum, or an able man condemned to "pulmonary tuberculosis," by removing a bleeding polypus. A large proportion of his cases of nerves, of deafness, of bronchitis, of gastritis, and of mere want of development of body or mind are nose cases and they cannot be neglected."

The book is attractively printed with numerous explanatory illustrations made by the author. Sylvan Rosenheim.

A Text-Book of Minor Surgery. By Edward Milton Foote, A. M., M. D., Instructor in Surgery, College of Physicians and Surgeons (Columbia University), etc. Illustrated. (*New York and London: D. Appleton & Co., 1908.*)

In reviewing Dr. Edward Milton Foote's text-book on Minor Surgery one is impressed with the systematic and logical arrangement of its contents. There is the same general outline for each chapter supplemented by descriptions of the lesions peculiar to the anatomical division of which it treats.

The book is an intensely practical one. Burns, bruises and sprains—their diagnosis, treatment and prognosis—are described in as much detail as herniæ and fractures of the femur. The chapter on surgical supplies is especially valuable, giving the prices of materials used and the most economical method of purchasing and preparing supplies.

Notwithstanding all its detail the book is interesting and one is constrained to read it through to the end in hopes of finding some useful hints, and he is not disappointed. The excellent plates all through the book add greatly to its value, especially in the chapter on bandaging, in which the many photographs show more clearly than words could describe the essential steps in the application of the more important bandages.

We cannot agree with Dr. Foote throughout in his description of surgical technique, but feel that the most careful attention should be given to asepsis even in minor surgery.

Clinical Lectures and Addresses on Surgery. By C. B. LOCKWOOD, Surgeon to St. Bartholomew's Hospital, London. Second edition. 307 pages. (*London: Oxford University Press, 1907.*)

This little book is made up of fifteen clinical lectures and addresses on surgery, and although the statements made do not in some instances coincide with the ideas at present accepted in this country, the lectures are full of useful information and good common-sense advice. It is surprising to note that chloroform is the anæsthetic of choice in our author's clinic, and he claims much better working results by its use. He lays great stress, and rightly so, on the value of immediate microscopic diagnosis of tumors during the course of operations, and cites cases in his own experience where such a diagnosis has been of vital importance to the patient. The sections on the Introduction to the Study of Clinical Surgery and on Clinical Reasoning would be of value to every student, and the entire series of lectures are interesting and well worth reading. J. S. D.

Why Worry? By GEORGE LINCOLN WALTON, M. D., Consulting Neurologist to the Massachusetts General Hospital. (*Philadelphia and London: J. B. Lippincott Company, 1908.*)

As a necessary result of the modern (?) ideas about patients suffering from neurasthenia, psychasthenia and other mental troubles, numerous works have appeared in the last two or three years dealing with the treatment of these conditions. Many have been written for the benefit of the public, and the volume before us is the latest one of the series, and one of the best. There are few of us who don't worry about little matters of no importance, and the worry reduces many of us to a pitiful state of nervous irritability and instability. The author shows clearly how harmful worry is and how easily it may be avoided, and "Why Worry" will prove of real help to many, if they will only try to follow the wise advice given. R. N.

BOOKS RECEIVED.

The Diseases of Children. Edited by Dr. M. Pfaundler and Dr. A. Schlossmann. English translation edited by Henry L. K. Shaw, M. D., and Linnaeus La Fétra, M. D. With an introduction by L. Emmett Holt, M. D. In four volumes. Illustrated in black and white and in colors by 61 full-page plates and 430 text cuts. 1908. 4to. J. B. Lippincott Company, Philadelphia and London.

Scientific Memoirs (New Series), No. 31. By Officers of the Medical and Sanitary Departments of the Government of India. *The Development of the Leishman-Donovan Parasite in Cimex Rotundatus. Second report.* By Captain W. S. Patton, M. B., I. M. S. 1908. 4to. 25 pages. Superintendent of Government Printing, Calcutta, India.

Righthandedness and Lefthandedness. With Chapters Treating of the Writing Posture, the Rule of the Road, etc. By George M. Gould, M. D. 1908. 12mo. 210 pages. J. B. Lippincott Company, Philadelphia and London.

Green's Encyclopedia and Dictionary of Medicine and Surgery. Volume IV, Gum-Resins to Intussusception. Volume V, Inulin to Lumbar-Puncture. 1907. 4to. W. T. Keener & Co., Chicago.

Why Worry? By George Lincoln Walton, M. D. 1908. 12mo. 275 pages. J. B. Lippincott Company, Philadelphia and New York.

The Harvey Lectures. Delivered under the auspices of the Harvey Society of New York. 1906-1907. By Prof. A. E. Wright, Prof. C. A. Herter, Prof. W. T. Porter, Prof. J. G. Adami, Dr. S. J. Meltzer, Prof. F. G. Benedict, Prof. E. B. Wilson, Prof. George S. Huntington, Prof. W. T. Councilman and Prof. Friedrich Müller. 1908. 8vo. 314 pages. J. B. Lippincott Company, Philadelphia and London.

Adenomyoma of the Uterus. By Thomas Stephen Cullen, Associate Professor of Gynæcology in the Johns Hopkins University, etc. Illustrated by Hermann Becker and August Horn. 1908. 4to. 270 pages. W. B. Saunders Company, Philadelphia and London.

Insomnia and Nerve Strain. By Henry S. Upson, M. D. With Skiagraphic Illustrations. 1908. 12mo. 142 pages. G. P. Putnam's Sons, New York and London.

Diseases of the Nose, Throat and Ear. Medical and Surgical. By William Lincoln Ballenger, M. D. Illustrated with 471 engravings and 16 plates. 1908. 8vo. 905 pages. Lea & Febiger, Philadelphia and New York.

Progressive Medicine. A Quarterly Digest of Advances, Discoveries and Improvements in the Medical and Surgical Sciences. Edited by Hobart Amory Hare, M. D., assisted by H. R. M. Landis, M. D. Volume II. June, 1908. 8vo. 352 pages. Lea & Febiger, Philadelphia and New York.

Diseases of the Nervous System. By H. Campbell Thomson, M. D. (Lond.), F. R. C. P. With 8 colored and 12 black-and-white plates, and 101 figures in the text. 1908. 12mo. 480 pages. W. T. Keener & Co., Chicago.

Electrical Treatment. By Wilfred Harris, M. D., F. R. C. P. Illustrated. 1908. 12mo. 383 pages. W. T. Keener & Co., Chicago.

A Text-Book of Surgical Anatomy. By William Francis Campbell, M. D. With 319 original illustrations. 1908. 8vo. 675 pages. W. B. Saunders Company, Philadelphia and London.

Bier's Hyperemic Treatment. In Surgery, Medicine and the Specialties. A Manual of its Practical Application. By Willy Meyer, M. D., and Professor Dr. Victor Schmeiden. Illustrated. 1908. 8vo. 209 pages. W. B. Saunders Company, Philadelphia and London.

A Manual of the Diseases of Infants and Children. By John Ruhräh, M. D. Second edition, thoroughly revised. 1908. 12mo. 423 pages. W. B. Saunders Company, Philadelphia and London.

State Board Questions and Answers. By P. Max Goepp, M. D. 1908. 8vo. 684 pages. W. B. Saunders Company, Philadelphia and London.

Pharmacology. The Action and Uses of Drugs. By Maurice Vejux Tyrode, M. D. 1908. 8vo. 255 pages. P. Blackiston's Son & Co., Philadelphia.

Meat and Food Inspection. By William Robertson, M. D., D. P. H. F. P. S. With *Regulations Governing Meat Inspection in the United States.* By Maximilian Herzog, M. D. 1908. 8vo. 388 pages. W. T. Keener & Co., Chicago.

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